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(54) Title: A METHOD FOR THE PROPHYLAXIS AND/OR TREATMENT OF PROLIFERATIVE AND/OR INFLAMMATORY SKIN DISORDERS

(57) Abstract

The present invention relates generally to a method for the prophylaxis and/or treatment of skin disorders, and in particular proliferative and/or inflammatory skin disorders, and to genetic molecules useful for same. The present invention is particularly directed to genetic molecules capable of modulating growth factor interaction with its receptor on epidermal keratinocytes to inhibit, reduce or otherwise decrease stimulation of this layer of cells. The present invention contemplates, in a most preferred embodiment, a method for the prophylaxis and/or treatment of psoriasis.

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A METHOD FOR THE PROPHYLAXIS AND/OR TREATMENT OF PROLIFERATIVE AND/OR INFLAMMATORY SKIN DISORDERS

5 The present invention relates generally to a method for the prophylaxis and/or treatment of skin disorders, and in particular proliferative and/or inflammatory skin disorders, and to genetic molecules useful for same. The present invention is particularly directed to genetic molecules capable of modulating growth factor interaction with its receptor on epidermal keratinocytes to inhibit, reduce or otherwise decrease stimulation of this layer
10 of cells. The present invention contemplates, in a most preferred embodiment, a method for the prophylaxis and/or treatment of psoriasis.

Bibliographic details of the publications numerically referred to in this specification are collected at the end of the description. Sequence Identity Numbers (SEQ ID NOs.) for
15 the nucleotide sequences referred to in the specification are defined following the bibliography.

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to
20 imply the inclusion of a stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of elements or integers.

Psoriasis and other similar conditions are common and often distressing proliferative and/or inflammatory skin disorders affecting or having the potential to affect a
25 significant proportion of the population. The condition arises from over proliferation of basal keratinocytes in the epidermal layer of the skin associated with inflammation in the underlying dermis. Whilst a range of treatments have been developed, none is completely effective and free of adverse side effects. Although the underlying cause of psoriasis remains elusive, there is some consensus of opinion that the condition arises
30 at least in part from over expression of local growth factors and their interaction with their receptors supporting keratinocyte proliferation *via* keratinocyte receptors which appear to be more abundant during psoriasis.

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One important group of growth factors are the dermally-derived insulin-like growth factors (IGFs) which support keratinocyte proliferation. In particular, IGF-I and IGF-II are ubiquitous peptides each with potent mitogenic effects on a broad range of cells. Molecules of the IGF type are also known as "progression factors" promoting
5 "competent" cells through DNA synthesis. The IGFs act through a common receptor known as the Type I or IGF-I receptor, which is tyrosine kinase linked. They are synthesised in mesenchymal tissues, including the dermis, and act on adjacent cells of mesodermal, endodermal or ectodermal origin. The regulation of their synthesis involves growth hormone (GH) in the liver, but is poorly defined in most tissues (1).

10

Particular proteins, referred to as IGF binding proteins (IGFBPs), appear to be involved in autocrine/paracrine regulation of tissue IGF availability (2). Six IGFBPs have so far been identified. The exact effects of the IGFBPs is not clear and observed effects *in vitro* have been inhibitory or stimulatory depending on the experimental method
15 employed (3). There is some evidence, however, that certain IGFBPs are involved in targeting IGF-I to its cell surface receptor.

Skin, comprising epidermis and underlying dermis, has GH receptors on dermal fibroblasts (4). Fibroblasts synthesize IGF-I as well as IGFBPs-3, -4, -5 and -6 (5) which
20 may be involved in targeting IGF-I to adjacent cells as well as to the overlying epidermis. The major epidermal cell type, the keratinocyte, does not synthesize IGF-I, but possesses IGF-I receptors and is responsive to IGF-I (6).

It is apparent, therefore, that IGF-I and other growth promoting molecules, are
25 responsible for or at least participate in a range of skin cell activities. In accordance with the present invention, the inventors have established that aberrations in the normal functioning of these molecules or aberrations in their interaction with their receptors is an important factor in proliferative and/or inflammatory skin disorders. It is proposed, therefore, to target these molecules or other molecules which facilitate their functioning
30 or interaction with their receptors to thereby ameliorate the effects of abberant activity during or leading to skin disease conditions.

Accordingly, one aspect of the present invention contemplates a method for ameliorating the effects of a proliferative and/or inflammatory skin disorder in a mammal, said method comprising contacting the proliferating and/or inflamed skin or skin capable of proliferation and/or inflammation with an effective amount of a nucleic acid molecule or chemical analogue thereof capable of inhibiting or otherwise reducing a growth factor mediated cell proliferation and/or inflammation.

Growth factor mediated cell proliferation and inflammation are also referred to as epidermal hyperplasias and may be mediated by any number of molecules such as but not limited to IGF-I, keratinocyte growth factor (KGF), transforming growth factor- α (TGF α), tumour necrosis factor- α (TNF α), interleukin-1, -4, -6 and 8 (IL-1, IL-4, IL-6 and IL-8, respectively), basic fibroblast growth factor (bFGF) or a combination of one or more of the above. The present invention is particularly described and exemplified with reference to IGF-I and its receptor (IGF-I receptor) and to IGF-I facilitating molecules, IGFBPs, since targeting these molecules according to the methods contemplated herein provides the best results to date. This is done, however, with the understanding that the present invention extends to any growth factor or cytokine-like molecule, a receptor thereof or a facilitating molecule like the IGFBPs involved in skin cell proliferation such as those molecules contemplated above and/or their receptors and/or facilitating molecules therefor.

According to this preferred embodiment, there is provided a method for ameliorating the effects of a proliferative and/or inflammatory skin disorder in a mammal, said method comprising contacting the proliferating and/or inflamed skin or skin capable of proliferation and/or inflammation with an effective amount of a nucleic acid molecule or chemical analogue thereof capable of inhibiting or otherwise reducing IGF-I mediated cell proliferation and/or inflammation.

The present invention is particularly described by psoriasis as the proliferative skin disorder. However, the subject invention extends to a range of proliferative and/or inflammatory skin disorders or epidermal hyperplasias such as but not limited to psoriasis, ichthyosis, pityriasis rubra pilaris ("PRP"), seborrhoea, keloids, keratoses,

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neoplasias and scleroderma, warts, benign growths and cancers of the skin.

In a preferred embodiment, therefore, the present invention is directed to a method for ameliorating the effects of psoriasis, said method comprising contacting proliferating
5 skin or skin capable of proliferation with an effective amount of a nucleic acid molecule or chemical analogue thereof capable of inhibiting or otherwise reducing IGF-I mediated cell proliferation.

The present invention extends to any mammal such as but not limited to humans,
10 livestock animals (e.g. horses, sheep, cows, goats, pigs, donkeys), laboratory test animals (e.g. rabbits, mice, guinea pigs), companion animals (e.g. cats, dogs) and captive wild animals. However, the instant invention is particularly directed to proliferative and/or inflammatory skin disorders such as psoriasis in humans.

15 The aspects of the subject invention instantly contemplated are particularly directed to the topical application of one or more suitable nucleic molecules capable of inhibiting, reducing or otherwise interfering with IGF-mediated cell proliferation and/or inflammation. More particularly, the nucleic acid molecule targets IGF-I interaction with its receptor. Conveniently, therefore, the nucleic acid molecule is an antagonist of
20 IGF-I interaction with its receptor. Most conveniently, the nucleic acid molecule antagonist is an antisense molecule to the IGF-I receptor, to IGF-I itself or to a molecule capable of facilitating IGF-I interaction with its receptor such as but not limited to an IGFBP.

25 Insofar as the invention relates to IGFBPs, the preferred molecules are IGFBP-2, -3, -4, -5 and -6. The most preferred molecules are IGFBP-2 and IGFBP-3.

The nucleotide sequences of IGFBP-2 and IGFBP-3 are set forth in Figures 1 (SEQ ID NO. 1) and 2 (SEQ ID NO. 2), respectively. According to a particularly preferred
30 aspect of the present invention, there is provided a nucleic acid molecule comprising at least about ten nucleotides capable of hybridising to, forming a heterodouplex or otherwise interacting with an mRNA molecule directed from a gene corresponding to

a genomic form of SEQ ID NO. 1 and/or SEQ ID NO. 2 and which thereby reduces or inhibits translation of said mRNA molecule. Preferably, the nucleic acid molecule is at least about 15 nucleotides in length and more preferably at least about 20-25 nucleotides in length. However, the instant invention extends to any length nucleic acid molecule
5 including a molecule of 100-200 nucleotides in length to correspond to the full length of or near full length of the subject genes.

The nucleotide sequence of the antisense molecules may correspond exactly to a region or portion of SEQ ID NO. 1 or SEQ ID NO. 2 or may differ by one or more nucleotide
10 substitutions, deletions and/or additions. It is a requirement, however, that the nucleic acid molecule interact with an mRNA molecule to thereby reduce its translation into active protein.

Examples of potential antisense molecules for IGFBP-2 and IGFBP-3 are those capable
15 of interacting with sequences selected from the lists in Examples 6 and 7, respectively.

The nucleic acid molecules in the form of an antisense molecule may be linear or covalently closed circular and single stranded or partially double stranded. A double stranded molecule may form a triplex with target mRNA or a target gene. The molecule
20 may also be protected from, for example, nucleases, by any number of means such as using a nonionic backbone or a phosphorothioate linkage. A convenient nonionic backbone contemplated herein is ethylphosphotriester linkage or a 2'-O-methylribosyl derivative.

25 Examples of suitable oligonucleotide analogues are conveniently described in Ts'O *et al* (7).

Alternatively, the antisense molecules of the present invention may target the IGF-I gene itself or its receptor or a multivalent antisense molecule may be constructed or separate
30 molecules administered which target at least two or an IGFBP, IGF-I and/or IGF-I-receptor. Examples of suitable antisense molecules capable of targetting the IGF-I receptor are those capable of interacting with sequences selected from the list in

Example 8. One particularly useful antisense molecule is

5'- ATCTCTCCGCTTCCTTTC -3' (SEQ ID NO. 10). A particularly preferred embodiment of the present invention contemplates a method of ameliorating the effects of psoriasis, said method comprising contacting proliferating skin or skin capable of proliferation with an effective amount of one or more nucleic acid molecules or chemical analogues thereof capable of inhibiting or otherwise reducing IGF-I mediated cell proliferation wherein said one or more molecules comprises a polynucleotide capable of interacting with mRNA directed from two or more of an IGF-I gene, an IGF-I receptor gene or a gene encoding an IGFBP such as IGFBP-2 and/or IGFBP-3.

10

In accordance with one aspect of the present invention the nucleic acid molecule is topically applied in aqueous solution or in conjunction with a cream, ointment, oil or other suitable carrier and/or diluent. A single application may be sufficient depending on the severity or exigencies of the condition although more commonly, multiple applications are required ranging from hourly, multi-hourly, daily, multi-daily, weekly or monthly, or in some other suitable time interval. The treatment might comprise solely the application of the nucleic acid molecule or this may be applied in conjunction with other treatments for the skin proliferation and/or inflammatory disorder being treated or for other associated conditions including microbial infection, bleeding and the formation of a variety of rashes.

20

As an alternative to or in conjunction with antisense therapy, the subject invention extends to the nucleic acid molecule as, or incorporating, a ribozyme including a minizyme to, for example, IGF-I, its receptor or to molecules such as IGFBPs and in particular IGFBP-2 and -3. Ribozymes are synthetic nucleic acid molecules which possess highly specific endoribonuclease activity. In particular, they comprise a hybridising region which is complementary in nucleotide sequence to at least part of a target RNA. Ribozymes are well described by Haseloff and Gerlach (8) and in International Patent Application No. WO 89/05852. The present invention extends to ribozymes which target mRNA specified by genes encoding IGF-I, its receptor or one or more IGFBPs such as IGFBP-2 and/or IGFBP-3.

30

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According to this embodiment, there is provided in a particularly preferred aspect a ribozyme comprising a hybridising region and a catalytic region wherein the hybridising region is capable of hybridising to at least part of a target mRNA sequence transcribed from a genomic gene corresponding to SEQ ID NO. 1 or SEQ ID NO. 2 wherein said
5 catalytic domain is capable of cleaving said target mRNA sequence to reduce or inhibit IGF-I mediated cell proliferation and/or inflammation.

Yet another aspect of the present invention contemplates co-suppression to reduce expression or to inhibit translation of an endogenous gene encoding, for example, IGF-I,
10 its receptor, or IGFBPs such as IGFBP-2 and/or -3. In co-suppression, a second copy of an endogenous gene or a substantially similar copy or analogue of an endogenous gene is introduced into a cell following topical administration. As with antisense molecules, nucleic acid molecules defining a ribozyme or nucleic acid molecules useful in co-suppression may first be protected such as by using a nonionic backbone.

15 The efficacy of the nucleic acid molecules of the present invention can be conveniently tested and screened using an *in vitro* system comprising a basal keratinocyte cell line. A particularly useful system comprises the HaCaT cell line described by Boukamp *et al* (9). In one assay, IGF-I is added to an oligonucleotide treated HaCaT cell line.
20 Alternatively, growth of oligonucleotide treated HaCaT cells is observed on a feeder layer of irradiated 3T3 fibroblasts. Using such *in vitro* assays, it is observed that antisense oligonucleotides to IGFBP-3, for example, inhibit production of IGFBP-3 by HaCaT cells. Other suitable animal models include the nude mouse/human skin graft model (15; 16) and the "flaky skin" mouse model (17; 18). In the nude mouse model,
25 microdermatome biopsies of psoriasis lesions are taken under local anaesthetic from volunteers then transplanted to congenital athymic (nude) mice. These transplanted human skin grafts maintain the characteristic hyperproliferating epidermis for 6-8 weeks. They are an established model for testing the efficacy of topically applied therapies for psoriasis. In the "flaky skin" mouse model, the *fsn/fsn* mutation produces mice with
30 skin resembling human psoriasis. This mouse, or another mutant mouse with a similar phenotype is a further *in vivo* model to test the efficacy of topically applied therapies for psoriasis.

Another aspect of the present invention contemplates a pharmaceutical composition for topical administration which comprises a nucleic acid molecule capable of inhibiting or otherwise reducing IGF-I mediated cell proliferation such as psoriasis and one or more pharmaceutically acceptable carriers and/or diluents. Preferably, the nucleic acid molecule is an antisense molecule to IGF-I, the IGF-I receptor or an IGFBP such as IGFBP-2 and/or IGFBP-3 or comprises a ribozyme to one or more of these targets or is a molecule suitable for co-suppression of one or more of these targets. The composition may comprise a single species of a nucleic acid molecule capable of targeting one of IGF-I, its receptor or an IGFBP, such as IGFBP-2 or IGFBP-3 or may be a multi-valent molecule capable of targeting two or more of IGF-I, its receptor or an IGFBP, such as IGFBP-2 and/or IGFBP-3.

The nucleic acid molecules may be administered in dispersions prepared in creams, ointments, oil or other suitable carrier and/or diluent such as glycerol, liquid polyethylene glycols and/or mixtures thereof. Under ordinary conditions of storage and use, these preparations may contain a preservative to prevent the growth of microorganisms.

The pharmaceutical forms suitable for topical use include sterile aqueous solutions (where water soluble) or dispersions and powders for the extemporaneous preparation of topical solutions or dispersion. In all cases, the form is preferably sterile although this is not an absolute requirement and is stable under the conditions of manufacture and storage. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof and vegetable oils. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. The prevention of the action of microorganism can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride.

Topical solutions are prepared by incorporating the nucleic acid molecule compound in the required amount in the appropriate solvent with various of the other ingredients enumerated above, as required, followed by where necessary filter sterilization.

- 5 As used herein "pharmaceutically acceptable carriers and/or diluents" include any and all solvents, dispersion media, aqueous solutions, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, use thereof
- 10 in the pharmaceutical compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. Conveniently, the nucleic acid molecules of the present invention are stored in freeze-dried form and are reconstituted prior to use.
- 15 Yet another aspect of the present invention contemplates the use of a nucleic acid molecule in the manufacture of a medicament for the treatment of proliferative and/or inflammatory skin disorders mediated by a growth factor. The proliferative and/or inflammatory skin disorder is generally psoriasis and the nucleic acid molecule targets IGF-I, the IGF-I receptor and/or an IGFBP such as IGFBP-2 and/or IGFBP-3.
- 20 Still a further aspect of the present invention contemplates an agent comprising a nucleic acid molecule as hereinbefore defined useful in the treatment of proliferative and/or inflammatory skin disorders, such as psoriasis.
- 25 The present invention is further described by the following non-limiting Figures and/or Examples.

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In the Figures:

Figure 1 is a representation of the nucleotide sequence of IGFBP-2.

```

5 LOCUS      HSIGFBP2      1433 bp      RNA      PRI      31-JAN-1990
   DEFINITION Human mRNA for insulin-like growth factor binding protein (IGFBP-2)
   ACCESSION  X16302
   KEYWORDS   insulin-like growth factor binding protein.
   SOURCE     human
10 ORGANISM   Homo sapiens
               Eukaryota; Animalia; Metazoa; Chordata; Vertebrata; Mammalia;
               Theria; Eutheria; Primates; Haplorhini; Catarrhini; Hominidae.
   REFERENCE  1 (bases 1 to 1433)
   AUTHORS    Binkert,C., Landwehr,J., Mary,J.L., Schwander,J. and Heinrich,G.
15 TITLE      Cloning, sequence analysis and expression of a cDNA encoding a
               novel insulin-like growth factor binding protein (IGFBP-2)
   JOURNAL    EMBO J. 8, 2497-2502 (1989)
   STANDARD   full automatic
   COMMENT     NCBI gi: 33009
20 FEATURES   Location/Qualifiers
               source          1. .1433
                               /organism="Homo sapiens"
                               /dev_stage="fetal"
                               /tissue_type="liver"
25             misc_feature    1416. .1420
                               /note="pot. polyadenylation signal"
               polyA_site      1433
                               /note="polyadenylation site"
               CDS              118. .1104
30                               /note="precursor polypeptide; (AA -39 to 289); NCBI gi:
                               33010."
                               /codon_start=1
                               /translation="MLPRVGC PALPLPPP LLLPLLLLLLGASGGGGGARA EVLFR
35 CPPCTPERLAACGPPPVAPPA AVAAVAGGARMPCAE LVREPGCGCCSVCARLEGEACG
VYTPRCGQLRCYPHPGSELPLQALVMGEGTCEKRRDAEYGASPEQVADNGDDHSEGG
LVENHVDSTMNMLGGGGSAGRKPLKSGMKELAVFREKVTEQHRQMGKGGKHHLGLEEP
KKLRPPP PARTPCQQELDQVLERISTMRLPDERGPLEHLYSLHIPNCDKHGLYNLKQCK
MSLNGQRGECWCVNPNNTGKLIQGAPTIRGDPECHLFYNEQQEACGVHTQRMQ"
               CDS              118. .234
40                               /note="signal peptide; (AA -39 to -1); NCBI gi: 33011."
                               /codon_start=1
                               /translation="MLPRVGC PALPLPPP LLLPLLLLLLGASGGGGGARA"
               CDS              235. .1101
45                               /note="mature IGFBP-2; (AA 1 to 289); NCBI gi: 33012."
                               /codon_start=1
                               /translation="EVLFRCPPCTPERLAACGPPPVAPPA AVAAVAGGARMPCAE LV
EPGCGCCSVCARLEGEACGVYTPRCGQLRCYPHPGSELPLQALVMGEGTCEKRRDAE
YGASPEQVADNGDDHSEGG LVENHVDSTMNMLGGGGSAGRKPLKSGMKELAVFREKVT
EQHRQMGKGGKHHLGLEEPKKLRPPP PARTPCQQELDQVLERISTMRLPDERGPLEHLY
50 SLHIPNCDKHGLYNLKQCKMSLNGQRGECWCVNPNNTGKLIQGAPTIRGDPECHLFYNE
QQEACGVHTQRMQ"
   BASE COUNT      239 a      466 c      501 g      227 t
   ORIGIN
55 HSIGFBP2 Length: 1433 May 11, 1994 10:06 Type: N Check: 6232 ..

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Figure 2 is a representation of the nucleotide sequence of IGFBP-3.

```

5  LOCUS      HUMGFIBPA      2474 bp ss-mRNA      PRI      15-JUN-1990
   DEFINITION Human growth hormone-dependent insulin-like growth factor-binding
               protein mRNA, complete cds.
   ACCESSION  M31159
   KEYWORDS   insulin-like growth factor binding protein.
   SOURCE     Human plasma, cDNA to mRNA, clone BP-53.
10  ORGANISM  Homo sapiens
               Eukaryota; Animalia; Chordata; Vertebrata; Mammalia; Theria;
               Eutheria; Primates; Haplorhini; Catarrhini; Hominidae.
   REFERENCE  1 (bases 1 to 2474)
15  AUTHORS   Wood, W.I., Cachianes, G., Henzel, W.J., Winslow, G.A., Spencer, S.A.,
               Hellmiss, R., Martin, J.L. and Baxter, R.C.
   TITLE      Cloning and expression of the growth hormone-dependent insulin-like
               growth factor-binding protein
   JOURNAL     Mol. Endocrinol. 2, 1176-1185 (1988)
20  STANDARD  full automatic
   COMMENT     NCBI gi: 183115
   FEATURES    Location/Qualifiers
               mRNA
               <1..2474
               /note="GFIBP mRNA"
25  CDS        110..985
               /gene="IGFBP1"
               /note="insulin-like growth factor-binding protein; NCBI
               gi: 183116."
               /codon_start=1
30  /translation="MQRARPTLWAAALTLLVLLRGPPVARAGASSGGLGPVVRCEPCD
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               PLQALLDGRGLCVNASAVSRLRAYLLPAPPAPGNASESEEDRSAGSVSPVSS'THRV
               SDPKFHLHSKI I I I I KKGHAKDSQRYKVDYESQSTDTQNFSSSESKRETEYGPCRREME
               DTLNHLKFLNLVLSPRGVHPNCDKKGFYKKKQCRPSKGRKRGFCWCVDKYGQPLPGYT
35  source     1..2474
               /organism="Homo sapiens"
   BASE COUNT 597 a      646 c      651 g      580 t
   ORIGIN
40  HUMGFIBPA Length: 2474 May 11, 1994 10:00 Type: N Check: 9946 ..

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Figure 3 is a representation of the nucleotide sequence of IGF-1-receptor.

```

45  LOCUS      HSIGFIRR      4989 bp      RNA      PRI      28-MAR-1991
   DEFINITION Human mRNA for insulin-like growth factor I receptor
   ACCESSION  X04434 M24599
   KEYWORDS   glycoprotein; insulin receptor;
50  insulin-like growth factor I receptor; membrane glycoprotein;
               receptor; tyrosine kinase.
   SOURCE     human
   ORGANISM  Homo sapiens
               Eukaryota; Animalia; Metazoa; Chordata; Vertebrata; Mammalia;
               Theria; Eutheria; Primates; Haplorhini; Catarrhini; Hominidae.
55  REFERENCE  1 (bases 1 to 4989)
   AUTHORS   Ullrich, A., Gray, A., Tam, A.W., Yang-Feng, T., Tsubokawa, M.,
               Collins, C., Henzel, W., Bon, T.L., Kathuria, S., Chen, E., Jakobs, S.,
               Francke, U., Ramachandran, J. and Fujita-Yamaguchi, Y.
   TITLE      Insulin-like growth factor I receptor primary structure: comparison

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with insulin receptor suggests structural dererminants that define functional specificity

JOURNAL EMBO J. 5, 2503-2512 (1986)

STANDARD full automatic

5 COMMENT NCBI gi: 33058

FEATURES Location/Qualifiers

source 1. .4989

/organism="Homo sapiens"

/tissue_type="placenta"

10 /clone_lib="(lamda)gt10"

/clone="(lambda)IGF-1-R.85, (lambda)IGF-1-R.76"

sig_peptide 32. .121

mat_peptide 122. .4132

/note="IGF-I receptor"

15 misc_feature 122. .2251

/note="alpha-subunit (AA 1 - 710)"

misc_feature 182. .190

/note="pot.N-linked glycosylation site (AA 21 - 23)"

20 misc_feature 335. .343

/note="pot.N-linked glycostlation site (AA 72 - 74)"

misc_feature 434. .442

/note="pot.N-linked glycostlation site (AA 105 - 107)"

misc_feature 761. .769

/note="pot.N-linked glycostlation site (AA 214 - 216)"

25 misc_feature 971. .979

/note="pot.N-linked glycostlation site (AA 284 - 286)"

misc_feature 1280. .1288

/note="pot.N-linked glycostlation site (AA 387 - 389)"

30 misc_feature 1343. .1351

/note="pot.N-linked glycosylation site (AA 408 - 410)"

misc_feature 1631. .1639

/note="pot.N-linked glycostlation site (AA 504 - 506)"

misc_feature 1850. .1858

/note="pot.N-linked glycosylation site (AA 577 - 579)"

35 misc_feature 1895. .1903

/note="pot.N-linked glycosylation site (AA 592 - 594)"

misc_feature 1949. .1957

/note="pot.N-linked glycosylation site (AA 610 - 612)"

40 misc_feature 2240. .2251

/note="putative proreceptor processing site (AA 707 - 710)"

misc_feature 2252. .4132

/note="beta-subunit (AA 711 - 1337)"

45 misc_feature 2270. .2278

/note="pot.N-linked glycosylation site (AA 717 - 719]"

misc_feature 2297. .2305

/note="pot.N-linked glycosylation site (AA 726 - 728)"

misc_feature 2321. .2329

/note="pot.N-linked glycosylation site (AA 734 - 736)"

50 misc_feature 2729. .2737

/note="pot.N-linked glycosylation site (AA 870 - 872)"

misc_feature 2768. .2776

/note="pot.N-linked glycosylation site (AA 883 - 885)"

misc_feature 2837. .2908

55 /note="transmembrane region (AA 906 - 929)"

misc_feature 2918. .2926

/note="pot.N-linked glycosylation site (AA 933 - 935)"

misc_feature 3047. .3049

/note="pot.ATP binding site (AA 976)"

60 misc_feature 3053. .3055

/note="pot.ATP binding site (AA 978)"

misc_feature 3062. .3064

/note="pot.ATP binding site (AA 981)"

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misc_feature      3128..3130
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                  /product="IGF-I receptor"
                  /note="50 stops when translation attempted, frame 1, code
5                  0"
BASE COUNT       1216 a   1371 c   1320 g   1082 t
ORIGIN
10  HSIGFIRR Length: 4989 May 11, 1994 12:10 Type: N Check: 133 ..

```

Figure 4A is a photographic representation of a Western ligand blot of HaCaT conditioned medium showing IGFBP-3 secreted in 24 hours after 7 day treatment with phosphorothioate oligonucleotides (BP3AS2, BP3AS3 and BP3S) at 0.5 μ M and 5 μ M;
 15 * no oligonucleotide added.

Figure 4B is a graphical representation of a scanning imaging densitometry of Western ligand blot (Figure 4A), showing relative band intensities of IGFBP-3 and the 24kDa
 20 IGFBP-4 after treatment with phosphorothioate oligonucleotides;
 * no oligonucleotide added.

Figure 5A is a photographic representation of a Western ligand blot of HaCaT conditioned medium showing IGFBP-3 secreted in 24 hours after 7 day treatment with
 25 phosphorothioate oligonucleotide BP3AS2 at 0.5 μ M compared with several control oligonucleotides at 0.5 μ M. (a) oligonucleotide BP3AS2NS; (b) oligonucleotide BP3AS4; (c) oligonucleotide BP3AS4NS; and (untreated), no oligonucleotide added.

Figure 5B is a graphical representation of a scanning imaging densitometry of Western
 30 ligand blot (Figure 5A), showing relative band intensities of IGFBP-3 after treatment with phosphorothioate oligonucleotides as in Figure 5A, showing IGFBP-3 band intensities expressed as a percentage of the average band intensity from conditioned medium of cells not treated with oligonucleotide.

35 **Figure 6** is a graphical representation showing inhibition of IGF-I binding by antisense oligonucleotides to IGF-I receptor. IGFR.AS: antisense; IGFR.S: sense.

Figure 7 is a graphical representation showing inhibition of IGFBP-3 production in culture medium following initial treatment with antisense oligonucleotides once daily over a 2 day period.

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Figure 8 is a graphical representation showing optimization of IGFBP-3 antisense oligonucleotide concentration as determined by relative IGFBP-3 concentration in culture medium.

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EXAMPLE 1

IN VITRO ASSAY: CELLS

The differentiated human keratinocyte cell line, HaCaT (9) was used in the *in vitro* assay. Cells at passage numbers 33 to 36 were maintained as monolayer cultures in 5% v/v CO₂ at 37°C in Keratinocyte-SFM (Gibco) containing EGF and bovine pituitary extract as supplied. Media containing foetal calf serum were avoided because of the high content of IGF-I binding proteins in serum.

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Feeder layer plates of lethally irradiated 3T3 fibroblasts were prepared exactly as described by Rheinwald and Green (10).

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EXAMPLE 2

IN VITRO ASSAY: THYMIDINE INCORPORATION ASSAY

Cells were grown to 4 days post confluence in 2cm² wells with daily medium changes of Keratinocyte-SFM, then the medium was changed to DMEM (Cytosystems, Australia), with the following additions: 25mM Hepes, 0.19% w/v, sodium bicarbonate, 0.03% w/v glutamine (Sigma Chemical Co, USA), 50IU/ml penicillin and 50µg/ml streptomycin (Flow Laboratories). After 24 hours, IGF-I or tIGF-I was added to triplicate wells, at the concentrations indicated, in 0.5ml fresh DMEM containing 0.02% v/v bovine serum albumin (Sigma molecular biology grade) and incubated for a further 21 hours. [³H]-Thymidine (0.1µCi/well) was then added and the cells incubated for a further 3 hours. The medium was then aspirated and the cells washed once with ice-cold PBS and twice with ice-cold 10% v/v TCA. The TCA-precipitated monolayers were

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then solubilized with 0.25M NaOH (200µl/well), transferred to scintillation vials and radioactivity determined by liquid scintillation counting (Pharmacia Wallac 1410 liquid scintillation counter).

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EXAMPLE 3

WESTERN LIGAND BLOTTING

HaCaT conditioned medium (250µl) was concentrated by adding 750µl cold ethanol, incubating at -20°C for 2 hours and centrifuging at 16,000g for 20 min at 4°C. The resulting pellet was air dried, resuspended thoroughly in non-reducing Laemmli sample
10 buffer, heated to 90°C for 5 minutes and separated on 12% w/v SDS-PAGE according to the method of Laemmli (1970). Separated proteins were electrophoretically transferred to nitrocellulose membrane (0.45mm, Schleicher and Schuell, Dassel, Germany) in a buffer containing 25mM Tris, 192mM glycine and 20% v/v methanol. IGFBPs were then visualised by the procedure of Hossenlopp *et al* (11), using [¹²⁵I]-
15 IGF-I, followed by autoradiography. Autoradiographs were scanned in a BioRad Model GS-670 Imaging Densitometer and band densities were determined using the Molecular Analyst program.

EXAMPLE 4

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ANTISENSE OLIGONUCLEOTIDES

Phosphorothioate oligodeoxynucleotides were synthesised by Bresatec, Adelaide, South Australia, Australia. The following antisense sequences were used: BP3AS2, 5'- GCG CCC GCT GCA TGA CGC CTG CAA C -3' (SEQ ID NO. 4), a 25mer complementary to the start codon region of the human IGFBP-3 mRNA; BP3AS3, 5'- CGG GCG GCT
25 CAC CTG GAG CTG GCG -3' (SEQ ID NO. 5), a 24mer complementary to the exon 1/intron 1 splice site; BP3AS4, 5'- AGG CGG CTG ACG GCA CTA -3' (SEQ ID NO. 6), an 18mer complementary to a region of the coding sequence lacking RNA secondary structure and oligonucleotide-dimer formation (using the computer software "OLIGO for PC"). Since BP3AS4 was found to be ineffective at inhibiting IGFBP-3 synthesis, it
30 was used as a control. The following additional control oligonucleotide sequences were used: BP3S, 5'- CAG GCG TCA TGC AGC GGG C -3' (SEQ ID NO. 7), an 18mer sense control sequence equivalent to the start codon region; BP3AS2NS, 5'- CGG AGA

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TGC CGC ATG CCA GCG CAG G -3' (SEQ ID NO. 8), a 25mer randomised sequence with the same GC content as BP3AS2; BP3AS4NS, 5'- GAC AGC GTC GGA GCG ATC -3' (SEQ ID NO. 9), an 18mer randomised sequence with the same GC content as BP3AS4NS. Design of the oligonucleotides was based on the human IGFBP-3 cDNA sequence of Spratt *et al* (12).

Cells were grown to one day post confluence in 2cm² wells with daily medium changes of 0.5ml Keratinocyte-SFM, then subjected to daily medium changes of Keratinocyte-SFM for a further 4 days. Daily additions of 0.5ml fresh Keratinocyte-SFM were then continued for a further 7 days, except that at the time of medium addition, 5µl oligonucleotide in PBS was added to give the final concentrations indicated, then the wells were shaken to mix the oligonucleotide. After the final addition, cells were incubated for 24 hours and the medium collected for assay of IGFBPs. Cells were then counted after trypsinisation in a Coulter Industrial D Counter, Coulter Bedfordshire, UK. Cell numbers after oligonucleotide treatment differed by less than 10%.

EXAMPLE 5

ANTISENSE OLIGONUCLEOTIDES INHIBIT IGFBP-3 SYNTHESIS

HaCaT cells secrete mainly IGFBP-3 (>95%), with the only other IGFBP detectable in HaCaT conditioned medium being IGFBP-4 (<5%). The effect on IGFBP-3 and IGFBP-4 synthesis of antisense oligonucleotides at two concentrations, 5µM and 0.5µM, was tested. Two oligonucleotides were used, BP3AS2 and BP3AS3, directed against the start site and the intron 1/exon 1 splice site, respectively of the IGFBP-3 mRNA. As a control, a sense oligonucleotide corresponding to the start site was used. As shown in Figures 4A and 4B, all oligonucleotides at 5µM caused a significant reduction of IGFBP-3 synthesis compared with untreated cells, however, the two antisense oligonucleotides inhibited IGFBP-3 synthesis of approximately 50% compared to the sense control (Figure 4B). The antisense oligonucleotide directed to the start codon appeared to be more effective of the two, the difference being more apparent at the lower concentration of 0.5µM. The cells of IGFBP-4 secreted by the HaCaT cells make photographic reproduction of the bands on Western ligand blots difficult, however densitometry measurements provide adequate relative quantitation. This resulted in the

significant observation that IGFBP-4 levels were unaffected by oligonucleotide addition to the cells, suggesting that the observed inhibitory effects on IGFBP-3 are specific.

To further investigate the inhibitory effects of the more effective of the two antisense oligonucleotides, BP3AS2, inhibition by this oligonucleotide at 0.5 μ M was compared with a number of control oligonucleotides, including one antisense oligonucleotide to IGFBP-3 that had proved to be ineffective at 0.5 μ M. As shown in Figures 5A and 5B, BP3AS2 was again inhibitory, resulting in levels of IGFBP-3 of approximately 50% of the most non-specifically inhibitory control oligonucleotide, the randomised equivalent of BP3AS2. The other control oligonucleotides caused no reduction in IGFBP-3 levels at 0.5 μ M, compared to untreated cells. Of possible significance is the fact that this control oligonucleotide, BP3AS2NS, like BP3AS2 itself, has the highest potential T_m of the three control oligonucleotides used in this experiment, enhancing the probability of non-specific base pairing with non-target mRNAs. However, the lack of inhibition of IGFBP-4 secretion by BP3AS2 suggests that this oligonucleotide is selective even compared with the most closely related protein likely to be present in this cell line.

EXAMPLE 6

ANTISENSE OLIGONUCLEOTIDES OF IGFBP2

Antisense oligonucleotides to IGFBP2 may be selected from molecules capable of interacting with one or more of the following sense oligonucleotides:

ATTCGGGGCGAGGGA	AAGAAGCGGAGGAGG	CCCGCTCGCAGGGCC
TTCGGGGCGAGGGAG	AGAAGCGGAGGAGGC	CCGCTCGCAGGGCCG
TCGGGGCGAGGGAGG	GAAGCGGAGGAGGCG	CGCTCGCAGGGCCGT
25 CGGGGCGAGGGAGGA	AAGCGGAGGAGGCGG	GCTCGCAGGGCCGTG
GGGGCGAGGGAGGAG	AGCGGAGGAGGCGGC	CTCGCAGGGCCGTGC
GGGCGAGGGAGGAGG	GCGGAGGAGGCGGCT	TCGCAGGGCCGTGCA
GGCGAGGGAGGAGGA	CGGAGGAGGCGGCTC	CGCAGGGCCGTGCAC
GCGAGGGAGGAGGAA	GGAGGAGGCGGCTCC	GCAGGGCCGTGCACC
30 CGAGGGAGGAGGAAG	GAGGAGGCGGCTCCC	CAGGGCCGTGCACCT
GAGGGAGGAGGAAGA	AGGAGGCGGCTCCCG	AGGGCCGTGCACCTG
AGGGAGGAGGAAGAA	GGAGGCGGCTCCCGC	GGGCCGTGCACCTGC
GGGAGGAGGAAGAAG	GAGGCGGCTCCCGCT	GGCCGTGCACCTGCC
GGAGGAGGAAGAAGC	AGGCGGCTCCCGCTC	GCCGTGCACCTGCC
35 GAGGAGGAAGAAGCG	GGCGGCTCCCGCTCG	CCGTGCACCTGCCCG
AGGAGGAAGAAGCGG	GCGGCTCCCGCTCGC	CGTGCACCTGCCCGC
GGAGGAAGAAGCGGA	CGGCTCCCGCTCGCA	GTGCACCTGCCCGCC
GAGGAAGAAGCGGAG	GGCTCCCGCTCGCAG	TGCACCTGCCCGCCC
AGGAAGAAGCGGAGG	GCTCCCGCTCGCAGG	CACCTGCCCGCCCCG
40 GGAAGAAGCGGAGGA	CTCCCGCTCGCAGGG	CACCTGCCCGCCCCG
GAAGAAGCGGAGGAG	TCCCGCTCGCAGGGC	ACCTGCCCGCCCCGC

	CCTGCCCCGCCCCGCC	CATGCTGCCGAGAGT	CGCTGCTGCCGCTGC
	CTGCCCCGCCCCGCCG	ATGCTGCCGAGAGTG	GCTGCTGCCGCTGCT
	TGCCCCGCCCCGCCGC	TGCTGCCGAGAGTGG	CTGCTGCCGCTGCTG
	GCCCCGCCCCGCCCCGCT	GCTGCCGAGAGTGGG	TGCTGCCGCTGCTGC
5	CCCCGCCCCGCCCCGCTC	CTGCCGAGAGTGGGC	GCTGCCGCTGCTGCT
	CCGCCCCGCCCCGCTCG	TGCCGAGAGTGGGCT	CTGCCGCTGCTGCTG
	CGCCCCGCCCCGCTCGC	GCCGAGAGTGGGCTG	TGCCGCTGCTGCTGC
	GCCCCGCCCCGCTCGCT	CCGAGAGTGGGCTGC	GCCGCTGCTGCTGCT
	CCCCGCCCCGCTCGCTC	CGAGAGTGGGCTGCC	CCGCTGCTGCTGCTG
10	CCGCCCCGCTCGCTCG	GAGAGTGGGCTGCCC	CGCTGCTGCTGCTGC
	CGCCCCGCTCGCTCGC	AGAGTGGGCTGCCCC	GCTGCTGCTGCTGCT
	GCCCCGCTCGCTCGCT	GAGTGGGCTGCCCCG	CTGCTGCTGCTGCTA
	CCCGCTCGCTCGCTC	AGTGGGCTGCCCCGC	TGCTGCTGCTGCTAC
	CCGCTCGCTCGCTCG	GTGGGCTGCCCCGCG	GCTGCTGCTGCTACT
15	CGCTCGCTCGCTCGC	TGGGCTGCCCCGCGC	CTGCTGCTGCTACTG
	GCTCGCTCGCTCGCC	GGGCTGCCCCGCGCT	TGCTGCTGCTACTGG
	CTCGCTCGCTCGCCC	GGCTGCCCCGCGCTG	GCTGCTGCTACTGGG
	TCGCTCGCTCGCCCC	GCTGCCCCGCGCTGC	CTGCTGCTACTGGGC
	CGCTCGCTCGCCCCG	CTGCCCCGCGCTGCC	TGCTGCTACTGGGCG
20	GCTCGCTCGCCCCGC	TGCCCCGCGCTGCCG	GCTGCTACTGGGCGC
	CTCGCTCGCCCCGCG	GCCCCGCGCTGCCGC	CTGCTACTGGGCGCG
	TCGCTCGCCCCGCGC	CCCCGCGCTGCCGCT	TGCTACTGGGCGCGA
	CGCTCGCCCCGCGCG	CCCGCGCTGCCGCTG	GCTACTGGGCGCGAG
	GCTCGCCCCGCGCGC	CCGCGCTGCCGCTGC	CTACTGGGCGCGAGT
25	CTCGCCCCGCGCGCC	CGCGCTGCCGCTGCC	TACTGGGCGCGAGTG
	TCGCCCCGCGCGCCG	GCGCTGCCGCTGCCG	ACTGGGCGCGAGTGG
	CGCCCCGCGCGCCGC	CGCTGCCGCTGCCGC	CTGGGCGCGAGTGGC
	GCCCCGCGCGCCGCG	GCTGCCGCTGCCGCC	TGGGCGCGAGTGGCG
	CCCGCCGCGCGCGCG	CTGCCGCTGCCGCCG	GGGCGCGAGTGGCGG
30	CCGCCGCGCGCGCT	TGCCGCTGCCGCCGC	GCGCGAGTGGCGGCG
	CGCCGCGCGCGCTG	GCCGCTGCCGCCGCC	CGCGAGTGGCGGCGG
	GCCGCGCGCGCTGC	CCGCTGCCGCCGCCG	GCGAGTGGCGGCGGC
	CCGCGCGCGCTGCC	CGTGCCGCCGCCGCC	CGAGTGGCGGCGGCG
	CGCGCGCGCTGCCG	CTGCCGCCGCCGCCG	GAGTGGCGGCGGCGG
35	GCGCGCGCTGCCGA	TGCCGCCGCCGCCGC	AGTGGCGGCGGCGGC
	CGCCGCGCTGCCGAC	GCCGCCGCCGCCGCT	GTGGCGGCGGCGGCG
	GCCGCGCTGCCGACC	CCGCCGCCGCCGCTG	TGGCGGCGGCGGCGG
	CCGCGCTGCCGACCG	CGCCGCCGCCGCTGC	GGCGGCGGCGGCGGG
	CGCGCTGCCGACCGC	GCCGCCGCCGCTGCT	GCGGCGGCGGCGGGG
40	GCGCTGCCGACCGCC	CCGCCGCCGCTGCTG	CGGCGGCGGCGGGGC
	CGCTGCCGACCGCCA	CGCCGCCGCTGCTGC	GGCGGCGGCGGGGCG
	GCTGCCGACCGCCAG	GCCGCCGCTGCTGCC	GCGGCGGCGGGGCGC
	CTGCCGACCGCCAGC	CCGCCGCTGCTGCCG	CGGCGGCGGGGCGCG
	TGCCGACCGCCAGCA	CGCCGCTGCTGCCGC	GGCGGCGGGGCGCGC
45	GCCGACCGCCAGCAT	GCCGCTGCTGCCGCT	GCGGCGGGGCGCGCG
	CCGACCGCCAGCATG	CCGCTGCTGCCGCTG	CGGCGGGGCGCGCGC
	CGACCGCCAGCATGC	CGCTGCTGCCGCTGC	GGCGGGGCGCGCGCG
	GACCGCCAGCATGCT	GCTGCTGCCGCTGCT	GCGGGGCGCGCGCGG
	ACCGCCAGCATGCTG	CTGCTGCCGCTGCTG	CGGGGCGCGCGCGGA
50	CCGCCAGCATGCTGC	TGCTGCCGCTGCTGC	GGGGCGCGCGCGGAG
	CGCCAGCATGCTGCC	GCTGCCGCTGCTGCC	GGGCGCGCGCGGAGG
	GCCAGCATGCTGCCG	CTGCCGCTGCTGCCG	GGCGCGCGCGGAGGT
	CCAGCATGCTGCCGA	TGCCGCTGCTGCCGC	GCGCGCGCGGAGGTG
	CAGCATGCTGCCGAG	GCCGCTGCTGCCGCT	CGCGCGCGGAGGTGC
55	AGCATGCTGCCGAGA	CCGCTGCTGCCGCTG	GCGCGCGGAGGTGCT
	GCATGCTGCCGAGAG		

	GCCCCGCTGGAGGGC	GCGCTGCTATCCCCA	AGGGCACTTGTGAGA
	CCCGGCTGGAGGGCG	CGCTGCTATCCCCAC	GGGCACTTGTGAGAA
	CCGGCTGGAGGGCGA	GCTGCTATCCCCACC	GGCACTTGTGAGAAG
	CGGCTGGAGGGCGAG	CTGCTATCCCCACCC	GCACTTGTGAGAAGC
5	GGCTGGAGGGCGAGG	TGCTATCCCCACCCG	CACTTGTGAGAAGCG
	GCTGGAGGGCGAGGC	GCTATCCCCACCCGG	ACTTGTGAGAAGCGC
	CTGGAGGGCGAGGCG	CTATCCCCACCCGGG	CTTGTGAGAAGCGCC
	TGGAGGGCGAGGCGT	TATCCCCACCCGGGC	TTGTGAGAAGCGCCG
	GGAGGGCGAGGCGTG	ATCCCCACCCGGGCT	TGTGAGAAGCGCCGG
10	GAGGGCGAGGCGTGC	TCCCCACCCGGGCTC	GTGAGAAGCGCCGGG
	AGGGCGAGGCGTGCG	CCCCACCCGGGCTCC	TGAGAAGCGCCGGGA
	GGGCGAGGCGTGCGG	CCCACCCGGGCTCCG	GAGAAGCGCCGGGAC
	GGCGAGGCGTGCGGC	CCACCCGGGCTCCGA	AGAAGCGCCGGGACG
	GCGAGGCGTGCGGCG	CACCCGGGCTCCGAG	GAAGCGCCGGGACGC
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	TGCGGCGTCTACACC	TCCGAGCTGCCCCTG	GGGACGCCGAGTATG
	GCGGCGTCTACACCC	CCGAGCTGCCCCCTG	GGACGCCGAGTATGG
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	GTCTACACCCCGCGC	CTGCCCCCTGCAGGCG	CCGAGTATGGCGCCA
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	CCGCGCTGCGGCCAG	CAGGCGCTGGTCATG	GCGCCAGCCCGGAGC
	CGCGCTGCGGCCAGG	AGGCGCTGGTCATGG	CGCCAGCCCGGAGCA
	GCGCTGCGGCCAGGG	GGCGCTGGTCATGGG	GCCAGCCCGGAGCAG
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	GCTGCGGCCAGGGGC	CGCTGGTCATGGGCG	CAGCCCGGAGCAGGT
	CTGCGGCCAGGGGCT	GCTGGTCATGGGCGA	AGCCCGGAGCAGGTT
	TGCGGCCAGGGGCTG	CTGGTCATGGGCGAG	GCCCGGAGCAGGTTG
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	CAATGGCGATGACCA	TGAACATGTTGGGCG	AAGGAGCTGGCCGTG
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	TGGCGATGACCACTC	ACATGTTGGGCGGGG	GAGCTGGCCGTGTTT
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	CGATGACCACTCAGA	TGTTGGGCGGGGGAG	CTGGCCGTGTTCCGG
	GATGACCACTCAGAA	GTTGGGCGGGGGAGG	TGGCCGTGTTCCGGG
	ATGACCACTCAGAAG	TTGGGCGGGGGAGGC	GGCCGTGTTCCGGGA
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	GACCACTCAGAAGGA	GGGCGGGGGAGGCAG	CCGTGTTCCGGGAGA
	ACCACTCAGAAGGAG	GGCGGGGGAGGCAGT	CGTGTTCCGGGAGAA
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	CACTCAGAAGGAGGC	CGGGGGAGGCAGTGC	TGTTCCGGGAGAAGG
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	CTCAGAAGGAGGCCT	GGGGAGGCAGTGCTG	TTCCGGGAGAAGGTC
	TCAGAAGGAGGCCTG	GGGAGGCAGTGCTGG	TCCGGGAGAAGGTCA
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	AGAAGGAGGCCTGGT	GAGGCAGTGCTGGCC	CGGGAGAAGGTCACT
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	AGGAGGCCTGGTGGA	GCAGTGCTGGCCGGA	GAGAAGGTCACTGAG
	GGAGGCCTGGTGAG	CAGTGCTGGCCGGAA	AGAAGGTCACTGAGC
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	CTGGTGAGAACCA	TGGCCGGAAGCCCCCT	TCACTGAGCAGCAC
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	TGGAGAACCA	CGGAAGCCCCCTCAAG	TGAGCAGCACCGGCA
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	GAACCACGTGGACAG	AGCCCCCTCAAGTCGG	CAGCACCGGCAGATG
	AACCACGTGGACAGC	GCCCCCTCAAGTCGGG	AGCACCGGCAGATGG
	ACCACGTGGACAGCA	CCCCCTCAAGTCGGGT	GCACCGGCAGATGGG
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	ACGTGGACAGCACCA	CTCAAGTCGGGTATG	CCGGCAGATGGGCAA
	CGTGGACAGCACCAT	TCAAGTCGGGTATGA	CGGCAGATGGGCAAG
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	GACAGCACCATGAAC	GTCGGGTATGAAGGA	AGATGGGCAAGGGTG
	ACAGCACCATGAACA	TCGGGTATGAAGGAG	GATGGGCAAGGGTGG
	CAGCACCATGAACAT	CGGGTATGAAGGAGC	ATGGGCAAGGGTGGC
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	GGGTGGCAAGCATCA	CCAGGACTCCCTGCC	CGCCTTCCGGATGAG
	GGTGGCAAGCATCAC	CAGGACTCCCTGCCA	GCCTTCCGGATGAGC
	GTGGCAAGCATCACC	AGGACTCCCTGCCAA	CCTTCCGGATGAGCG
	TGGCAAGCATCACCT	GGA CTCCCTGCCAAC	CTTCCGGATGAGCGG
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	GCAAGCATCACCTTG	ACTCCCTGCCAACAG	TCCGGATGAGCGGGG
	CAAGCATCACCTTGG	CTCCCTGCCAACAGG	CCGGATGAGCGGGGC
	AAGCATCACCTTGGC	TCCCTGCCAACAGGA	CGGATGAGCGGGGCC
	AGCATCACCTTGGCC	CCCTGCCAACAGGAA	GGATGAGCGGGGGCCC
15	GCATCACCTTGGCCT	CCTGCCAACAGGAAC	GATGAGCGGGGGCCCT
	CATCACCTTGGCCTG	CTGCCAACAGGAACT	ATGAGCGGGGGCCCTC
	ATCACCTTGGCCTGG	TGCCAACAGGAACTG	TGAGCGGGGGCCCTCT
	TCACCTTGGCCTGGA	GCCAACAGGAACTGG	GAGCGGGGGCCCTCTG
	CACCTTGGCCTGGAG	CCAACAGGAACTGGA	AGCGGGGGCCCTCTGG
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	CCTTGGCCTGGAGGA	AACAGGAACTGGACC	CGGGGGCCCTCTGGAG
	CTTGGCCTGGAGGAG	ACAGGAACTGGACCA	GGGGCCCTCTGGAGC
	TTGGCCTGGAGGAGC	CAGGAACTGGACCAG	GGGCCCTCTGGAGCA
	TGGCCTGGAGGAGCC	AGGAACTGGACCAGG	GGCCCTCTGGAGCAC
25	GGCCTGGAGGAGCCC	GGA ACTGGACCAGGT	GCCCTCTGGAGCACC
	GCCTGGAGGAGCCCA	GA ACTGGACCAGGTC	CCCTCTGGAGCACCT
	CCTGGAGGAGCCCAA	AACTGGACCAGGTCC	CCTCTGGAGCACCTC
	CTGGAGGAGCCCAAG	ACTGGACCAGGTCCT	CTCTGGAGCACCTCT
	TGGAGGAGCCCAAGA	CTGGACCAGGTCCTG	TCTGGAGCACCTCTA
30	GGAGGAGCCCAAGAA	TGGACCAGGTCCTGG	CTGGAGCACCTCTAC
	GAGGAGCCCAAGAAG	GGACCAGGTCCTGGA	TGGAGCACCTCTACT
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	GGAGCCCAAGAAGCT	ACCAGGTCCTGGAGC	GAGCACCTCTACTCC
	GAGCCCAAGAAGCTG	CCAGGTCCTGGAGCG	AGCACCTCTACTCCC
35	AGCCCAAGAAGCTGC	CAGGTCCTGGAGCGG	GCACCTCTACTCCCT
	GCCCAAGAAGCTGCG	AGGTCCTGGAGCGGA	CACCTCTACTCCCTG
	CCCAAGAAGCTGCGA	GGTCCTGGAGCGGAT	ACCTCTACTCCCTGC
	CCAAGAAGCTGCGAC	GTCCTGGAGCGGATC	CCTCTACTCCCTGCA
	CAAGAAGCTGCGACC	TCCTGGAGCGGATCT	CTCTACTCCCTGCAC
40	AAGAAGCTGCGACCA	CCTGGAGCGGATCTC	TCTACTCCCTGCACA
	AGAAGCTGCGACCAC	CTGGAGCGGATCTCC	CTACTCCCTGCACAT
	GAAGCTGCGACCACC	TGGAGCGGATCTCCA	TACTCCCTGCACATC
	AAGCTGCGACCACCC	GGAGCGGATCTCCAC	ACTCCCTGCACATCC
	AGCTGCGACCACCCC	GAGCGGATCTCCACC	CTCCCTGCACATCCC
45	GCTGCGACCACCCCCT	AGCGGATCTCCACCA	TCCCTGCACATCCCC
	CTGCGACCACCCCCTG	GCGGATCTCCACCAT	CCCTGCACATCCCCA
	TGCGACCACCCCCTGC	CGGATCTCCACCATG	CCTGCACATCCCCAA
	GCGACCACCCCCTGCC	GGATCTCCACCATGC	CTGCACATCCCCAAC
	CGACCACCCCCTGCCA	GATCTCCACCATGCG	TGCACATCCCCAACT
50	GACCACCCCCTGCCA	ATCTCCACCATGCGC	GCACATCCCCAACTG
	ACCACCCCCTGCCAG	TCTCCACCATGCGCC	CACATCCCCAACTGT
	CCACCCCCTGCCAGG	CTCCACCATGCGCCT	ACATCCCCAACTGTG
	CACCCCCTGCCAGGA	TCCACCATGCGCCTT	CATCCCCAACTGTGA
	ACCCCCTGCCAGGAC	CCACCATGCGCCTTC	ATCCCCAACTGTGAC
55	CCCCCTGCCAGGACT	CACCATGCGCCTTCC	TCCCCAACTGTGACA
	CCCCTGCCAGGACTC	ACCATGCGCCTTCCG	CCCCAACTGTGACAA

	CCCAACTGTGACAAG	CGGGCAGCGTGGGGA	GAGCCCCCACCATCC
	CCAAGTGTGACAAGC	GGGCAGCGTGGGGAG	AGCCCCCACCATCCG
	CAACTGTGACAAGCA	GGCAGCGTGGGGAGT	GCCCCCACCATCCGG
	AACTGTGACAAGCAT	GCAGCGTGGGGAGTG	CCCCCACCATCCGGG
5	ACTGTGACAAGCATG	CAGCGTGGGGAGTGC	CCCCCACCATCCGGGG
	CTGTGACAAGCATGG	AGCGTGGGGAGTGCT	CCCACCATCCGGGGG
	TGTGACAAGCATGGC	GCGTGGGGAGTGCTG	CCACCATCCGGGGGG
	GTGACAAGCATGGCC	CGTGGGGAGTGCTGG	CACCATCCGGGGGGGA
	TGACAAGCATGGCCT	GTGGGGAGTGCTGGT	ACCATCCGGGGGGGAC
10	GACAAGCATGGCCTG	TGGGGAGTGCTGGTG	CCATCCGGGGGGGACC
	ACAAGCATGGCCTGT	GGGGAGTGCTGGTGT	CATCCGGGGGGGACCC
	CAAGCATGGCCTGTA	GGGAGTGCTGGTGTG	ATCCGGGGGGGACCCC
	AAGCATGGCCTGTAC	GGAGTGCTGGTGTGT	TCCGGGGGGGACCCCG
	AGCATGGCCTGTACA	GAGTGCTGGTGTGTG	CCGGGGGGGACCCCGA
15	GCATGGCCTGTACAA	AGTGCTGGTGTGTGA	CGGGGGGACCCCGAG
	CATGGCCTGTACAAC	GTGCTGGTGTGTGAA	GGGGGGGACCCCGAGT
	ATGGCCTGTACAACC	TGCTGGTGTGTGAAC	GGGGGACCCCGAGTG
	TGGCCTGTACAACCT	GCTGGTGTGTGAACC	GGGGACCCCGAGTGT
	GGCCTGTACAACCTC	CTGGTGTGTGAACCC	GGGACCCCGAGTGTC
20	GCCTGTACAACCTCA	TGGTGTGTGAACCCC	GGACCCCGAGTGTCAT
	CCTGTACAACCTCAA	GGTGTGTGAACCCCA	GACCCCGAGTGTCATC
	CTGTACAACCTCAAA	GTGTGTGAACCCCAA	ACCCCGAGTGTCATC
	TGTACAACCTCAAAC	TGTGTGAACCCCAAC	CCCCGAGTGTCATCT
	GTACAACCTCAAACA	GTGTGAACCCCAACA	CCCGAGTGTCATCTC
25	TACAACCTCAAACAG	TGTGAACCCCAACAC	CCGAGTGTCATCTCT
	ACAACCTCAAACAGT	GTGAACCCCAACACC	CGAGTGTCATCTCTT
	CAACCTCAAACAGTG	TGAACCCCAACACCG	GAGTGTCATCTCTTCT
	AACCTCAAACAGTGC	GAACCCCAACACCGG	AGTGTCATCTCTTCTA
	ACCTCAAACAGTGCA	AACCCCAACACCGGG	GTGTCATCTCTTCTAC
30	CCTCAAACAGTGCAA	ACCCCAACACCGGGA	GTCATCTCTTCTACAA
	CTCAAACAGTGCAAG	CCCCAACACCGGGAA	TCATCTCTTCTACAA
	TCAAACAGTGCAAGA	CCCAACACCGGGGAAG	CATCTCTTCTACAAT
	CAAACAGTGCAAGAT	CCAACACCGGGGAAGC	ATCTCTTCTACAATG
35	AAACAGTGCAAGATG	CAACACCGGGGAAGCT	TCTCTTCTACAATGA
	AACAGTGCAAGATGT	AACACCGGGGAAGCTG	CTCTTCTACAATGAG
	ACAGTGCAAGATGTC	ACACCGGGGAAGCTGA	TCTTCTACAATGAGC
	CAGTGCAAGATGTCT	CACCGGGGAAGCTGAT	CTTCTACAATGAGCA
	AGTGCAAGATGTCTC	ACCGGGGAAGCTGATC	TTCTACAATGAGCAG
40	GTGCAAGATGTCTCT	CCGGGAAGCTGATCC	TCTACAATGAGCAGC
	TGCAAGATGTCTCTG	CGGGAAGCTGATCCA	CTACAATGAGCAGCA
	GCAAGATGTCTCTGA	GGGAAGCTGATCCAG	TACAATGAGCAGCAG
	CAAGATGTCTCTGAA	GGAAGCTGATCCAGG	ACAATGAGCAGCAGG
	AAGATGTCTCTGAAC	GAAGCTGATCCAGGG	CAATGAGCAGCAGGA
45	AGATGTCTCTGAACG	AAGCTGATCCAGGGAG	AATGAGCAGCAGGAG
	GATGTCTCTGAACGG	AGCTGATCCAGGGAGC	ATGAGCAGCAGGAGG
	ATGTCTCTGAACGGG	GCTGATCCAGGGAGC	TGAGCAGCAGGAGGC
	TGTCTCTGAACGGGC	CTGATCCAGGGAGCCC	GAGCAGCAGGAGGCT
	GTCTCTGAACGGGCA	TGATCCAGGGAGCCCC	AGCAGCAGGAGGCTT
50	TCTCTGAACGGGCAG	GATCCAGGGAGCCCCC	GCAGCAGGAGGCTTG
	CTCTGAACGGGCAGC	ATCCAGGGAGCCCCC	CAGCAGGAGGCTTGC
	TCTGAACGGGCAGCG	TCCAGGGAGCCCCCA	AGCAGGAGGCTTGCG
	CTGAACGGGCAGCGT	CCAGGGAGCCCCCAC	GCAGGAGGCTTGCGG
	TGAACGGGCAGCGTG	CAGGGAGCCCCCACC	CAGGAGGCTTGCGGG
55	GAACGGGCAGCGTGG	AGGGAGCCCCCACC	AGGAGGCTTGCGGGG
	AACGGGCAGCGTGGG	GGGAGCCCCCACCAT	GGAGGCTTGCGGGGT
	ACGGGCAGCGTGGGG	GGAGCCCCCACCATC	

5	GAGGCTTGCGGGGTG AGGCTTGCGGGGTGC GGCTTGCGGGGTGCA GCTTGCGGGGTGCAC CTTGCGGGGTGCACA TTGCGGGGTGCACAC TGCGGGGTGCACACC GCGGGGTGCACACCC CGGGGTGCACACCCA 10 GGGGTGCACACCCAG GGGTGCACACCCAGC GGTGCACACCCAGCG GTGCACACCCAGCGG TGCACACCCAGCGGA 15 GCACACCCAGCGGAT CACACCCAGCGGATG ACACCCAGCGGATGC CACCCAGCGGATGCA ACCCAGCGGATGCAG 20 CCCAGCGGATGCAGT CCAGCGGATGCAGTA CAGCGGATGCAGTAG AGCGGATGCAGTAGA GCGGATGCAGTAGAC 25 CGGATGCAGTAGACC GGATGCAGTAGACCG GATGCAGTAGACCGC ATGCAGTAGACCGCA TGCAGTAGACCGCAG 30 GCAGTAGACCGCAGC CAGTAGACCGCAGCC AGTAGACCGCAGCCA GTAGACCGCAGCCAG TAGACCGCAGCCAGC 35 AGACCGCAGCCAGCC GACCGCAGCCAGCCG ACCGCAGCCAGCCGG CCGCAGCCAGCCGGT CGCAGCCAGCCGGTG 40 GCAGCCAGCCGGTGC CAGCCAGCCGGTGCC AGCCAGCCGGTGCCCT GCCAGCCGGTGCCCTG CCAGCCGGTGCCCTGG 45 CAGCCGGTGCCCTGGC AGCCGGTGCCCTGGCG GCCGGTGCCCTGGCGC CCGGTGCCCTGGCGCC CGGTGCCTGGCGCCC 50 GGTGCCTGGCGCCCC GTGCCTGGCGCCCCCT TGCCCTGGCGCCCCCTG GCCTGGCGCCCCCTGC CCTGGCGCCCCCTGCC 55 CTGGCGCCCCCTGCCC TGGCGCCCCCTGCCCC	GGCGCCCCCTGCCCCC GCGCCCCCTGCCCCCC CGCCCCCTGCCCCCCG GCCCCCTGCCCCCCCG CCCCCTGCCCCCCCGC CCCCCTGCCCCCCCGCC CCCTGCCCCCCCGCCC CCTGCCCCCCCGCCCC CTGCCCCCCCGCCCCCT TGCCCCCCCGCCCCCTC GCCCCCCCGCCCCCTCT CCCCCCCGCCCCCTCTC CCCCCGCCCCCTCTCC CCCCGCCCCCTCTCCA CCCGCCCCCTCTCCAA CCGCCCCCTCTCCAAA CGCCCCCTCTCCAAAC GCCCCCTCTCCAAACA CCCCCTCTCCAAACAC CCCTCTCCAAACACC CCTCTCCAAACACCG CTCTCCAAACACCGG TCTCCAAACACCGGC CTCCAAACACCGGCA TCCAAACACCGGCAG CCAAACACCGGCAGA CAAACACCGGCAGAA AAACACCGGCAGAAA AACACCGGCAGAAAA ACACCGGCAGAAAAAC CACCGGCAGAAAAACG ACCGGCAGAAAAACGG CCGGCAGAAAAACGGA CGGCAGAAAAACGGAG GGCAGAAAAACGGAGA GCAGAAAAACGGAGAG CAGAAAAACGGAGAGT AGAAAAACGGAGAGTG GAAAAACGGAGAGTGC AAAACGGAGAGTGCT AAACGGAGAGTGCTT AACGGAGAGTGCTTG ACGGAGAGTGCTTGG CGGAGAGTGCTTGGG GGAGAGTGCTTGGGT GAGAGTGCTTGGGTG AGAGTGCTTGGGTGG GAGTGCTTGGGTGGT AGTGCTTGGGTGGTG GTGCTTGGGTGGTGG TGCTTGGGTGGTGGG GCTTGGGTGGTGGGT CTTGGGTGGTGGGTG TTGGGTGGTGGGTGC TGGGTGGTGGGTGCT GGGTGGTGGGTGCTG GGTGGTGGGTGCTGG	GTGGTGGGTGCTGGA TGGTGGGTGCTGGAG GGTGGGTGCTGGAGG GTGGGTGCTGGAGGA TGGGTGCTGGAGGAT GGGTGCTGGAGGATT GGTGCTGGAGGATTT GTGCTGGAGGATTTT TGCTGGAGGATTTTTC GCTGGAGGATTTTTC CTGGAGGATTTTCCA TGGAGGATTTTCCAG GGAGGATTTTCCAGT GAGGATTTTCCAGTT AGGATTTTCCAGTTC GGATTTTCCAGTTCT GATTTTCCAGTTCTG ATTTTCCAGTTCTGA TTTTCCAGTTCTGAC TTTCCAGTTCTGACA TTCCAGTTCTGACAC TCCAGTTCTGACACA CCAGTTCTGACACAC CAGTTCTGACACACG AGTTCTGACACACGT GTTCTGACACACGTA TTCTGACACACGTAT TCTGACACACGTATT CTGACACACGTATTT TGACACACGTATTTA GACACACGTATTTAT ACACACGTATTTATA CACACGTATTTATAT ACACGTATTTATATT CACGTATTTATATTT ACGTATTTATATTTG CGTATTTATATTTGG GTATTTATATTTGGA TATTTATATTTGGAA ATTTATATTTGGAAA TTTATATTTGGAAAG TTATATTTGGAAAGA TATATTTGGAAAGAG ATATTTGGAAAGAGA TATTTGGAAAGAGAC ATTTGGAAAGAGACC TTTGGAAAGAGACCA TTGGAAAGAGACCAG TGGAAAGAGACCAGC GGAAAGAGACCAGCA GAAAGAGACCAGCAC AAAGAGACCAGCACC AAGAGACCAGCACCG AGAGACCAGCACCGA GAGACCAGCACCGAG AGACCAGCACCGAGC
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	GACCAGCACCGAGCT	CACCTGCTCCTTCTT	GGGTACAGGTTTGGG
	ACCAGCACCGAGCTC	ACCTGCTCCTTCTTG	GGTACAGGTTTGGGG
	CCAGCACCGAGCTCG	CCTGCTCCTTCTTGC	GTACAGGTTTGGGGA
	CAGCACCGAGCTCGG	CTGCTCCTTCTTGCT	TACAGGTTTGGGGAG
5	AGCACCGAGCTCGGC	TGCTCCTTCTTGCTT	ACAGGTTTGGGGAGG
	GCACCGAGCTCGGCA	GCTCCTTCTTGCTTT	CAGGTTTGGGGAGGG
	CACCGAGCTCGGCAC	CTCCTTCTTGCTTTC	AGGTTTGGGGAGGGG
	ACCGAGCTCGGCACC	TCCTTCTTGCTTTCC	GGTTTGGGGAGGGGG
	CCGAGCTCGGCACCT	CCTTCTTGCTTTCCC	GTTTGGGGAGGGGGA
10	CGAGCTCGGCACCTC	CTTCTTGCTTTCCCC	TTTGGGGAGGGGGAA
	GAGCTCGGCACCTCC	TTCTTGCTTTCCCCG	TTGGGGAGGGGGGAAG
	AGCTCGGCACCTCCC	TCTTGCTTTCCCCGC	TGGGGAGGGGGGAAGA
	GCTCGGCACCTCCCC	CTTGCTTTCCCCGGG	GGGGAGGGGGGAAGAG
	CTCGGCACCTCCCCG	TTGCTTTCCCCGGGG	GGGAGGGGGGAAGAGA
15	TCGGCACCTCCCCGG	TGCTTTCCCCGGGGG	GGAGGGGGGAAGAGAA
	CGGCACCTCCCCGGC	GCTTTCCCCGGGGGA	GAGGGGGAAGAGAAA
	GGCACCTCCCCGGCC	CTTTCCCCGGGGGAG	AGGGGGAAGAGAAAT
	GCACCTCCCCGGCCT	TTTCCCCGGGGGAGG	GGGGGAAGAGAAATT
	CACCTCCCCGGCCTC	TTCCCCGGGGGAGGA	GGGGAAGAGAAATTT
20	ACCTCCCCGGCCTCT	TCCCCGGGGGAGGAA	GGGAAGAGAAATTTT
	CCTCCCCGGCCTCTC	CCCCGGGGGAGGAAG	GGAAGAGAAATTTT
	CTCCCCGGCCTCTCT	CCCGGGGGAGGAAGG	GAAGAGAAATTTTAT
	TCCCCGGCCTCTCTC	CCGGGGGAGGAAGGG	AAGAGAAATTTTAT
	CCCCGGCCTCTCTCT	CGGGGGAGGAAGGGG	AGAGAAATTTTATTT
25	CCCGGCCTCTCTCTT	GGGGGAGGAAGGGGG	GAGAAATTTTATTTT
	CCGGCCTCTCTCTTC	GGGGAGGAAGGGGGT	AGAAATTTTATTTT
	CGGCCTCTCTCTTCC	GGGAGGAAGGGGGTT	GAAATTTTATTTT
	GGCCTCTCTCTTCCC	GGAGGAAGGGGGTTG	AAATTTTATTTT
	GCCTCTCTCTTCCCA	GAGGAAGGGGGTTGT	AATTTTATTTTGA
30	CCTCTCTCTTCCCAG	AGGAAGGGGGTTGTG	ATTTTATTTTGAAC
	CTCTCTCTTCCCAGC	GGAAGGGGGTTGTGG	TTTTATTTTGAACC
	TCTCTCTTCCCAGCT	GAAGGGGGTTGTGGT	TTTATTTTGAACCC
	CTCTCTTCCCAGCTG	AAGGGGGTTGTGGTC	TTATTTTGAACCCC
35	TCTCTTCCCAGCTGC	AGGGGGTTGTGGTCG	TATTTTGAACCCCT
	CTCTTCCCAGCTGCA	GGGGGTTGTGGTCGG	ATTTTGAACCCCTG
	TCTTCCCAGCTGCAG	GGGGTTGTGGTCGGG	TTTTTGAACCCCTGT
	CTTCCCAGCTGCAGA	GGTGTGTGGTCGGGG	TTTTGAACCCCTGTG
	TTCCCAGCTGCAGAT	GTTGTGGTCGGGGAG	TTTGAACCCCTGTGT
	TCCCAGCTGCAGATG	TTGTGGTCGGGGAGC	TTGAACCCCTGTGTC
40	CCCAGCTGCAGATGC	TGTGGTCGGGGAGCT	TGAACCCCTGTGTCC
	CCAGCTGCAGATGCC	GTGGTCGGGGAGCTG	GAACCCCTGTGTCCC
	CAGCTGCAGATGCCA	TGGTCGGGGAGCTGG	AACCCCTGTGTCCCT
	AGCTGCAGATGCCAC	GGTCGGGGAGCTGGG	ACCCCTGTGTCCCTT
45	GCTGCAGATGCCACA	GTCGGGGAGCTGGGG	CCCCTGTGTCCCTTT
	CTGCAGATGCCACAC	TCGGGGAGCTGGGGT	CCCTGTGTCCCTTTT
	TGCAGATGCCACACC	CGGGGAGCTGGGGTA	CCTGTGTCCCTTTTG
	GCAGATGCCACACCT	GGGGAGCTGGGGTAC	CTGTGTCCCTTTTGC
	CAGATGCCACACCTG	GGGAGCTGGGGTACA	TGTGTCCCTTTTGCAT
50	AGATGCCACACCTGC	GGAGCTGGGGTACAG	TGTCCCTTTTGCATA
	GATGCCACACCTGCT	GAGCTGGGGTACAGG	GTCCCTTTTGCATAA
	ATGCCACACCTGCTC	AGCTGGGGTACAGGT	TCCCTTTTGCATAAG
	TGCCACACCTGCTCC	GCTGGGGTACAGGTT	CCCTTTTGCATAAGA
	GCCACACCTGCTCCT	CTGGGGTACAGGTTT	CCTTTTGCATAAGAT
55	CCACACCTGCTCCTT	TGGGGTACAGGTTTG	CTTTTGCATAAGATT
	CACACCTGCTCCTTC	GGGGTACAGGTTTGG	
	ACACCTGCTCCTTCT		

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TTTTGCATAAGATTA
 TTTGCATAAGATTAA
 TTGCATAAGATTAAA
 TGCATAAGATTAAAG
 5 GCATAAGATTAAAGG
 CATAAGATTAAAGGA
 ATAAGATTAAAGGAA
 TAAGATTAAAGGAAG
 AAGATTAAAGGAAGG
 10 AGATTAAAGGAAGGA
 GATTAAAGGAAGGAA
 ATTAAAGGAAGGAAA
 TTAAAGGAAGGAAAA
 TAAAGGAAGGAAAAG
 15 AAAGGAAGGAAAAGT

EXAMPLE 7

ANTISENSE OLIGONUCLEOTIDES OF IGFBP3

20 Antisense oligonucleotides to IGFBP3 may be selected from molecules capable of interacting with one or more of the following sense oligonucleotides:

CTCAGCGCCCAGCCG	CCACAGCTTCGCGCC	ATCCCTGCGCGCCCA
TCAGCGCCCAGCCGC	CACAGCTTCGCGCCG	TCCCTGCGCGCCCAG
25 CAGCGCCCAGCCGCT	ACAGCTTCGCGCCGT	CCCTGCGCGCCCAGC
AGCGCCCAGCCGCTT	CAGCTTCGCGCCGTG	CCTGCGCGCCCAGCC
GCGCCCAGCCGCTTC	AGCTTCGCGCCGTGT	CTGCGCGCCCAGCCT
CGCCCAGCCGCTTCC	GCTTCGCGCCGTGTA	TGCGCGCCCAGCCTG
GCCCAGCCGCTTCCT	CTTCGCGCCGTGTAC	GCGCGCCCAGCCTGC
30 CCCAGCCGCTTCCTG	TTCGCGCCGTGTACT	CGCGCCCAGCCTGCC
CCAGCCGCTTCCTGC	TCGCGCCGTGTACTG	GCGCCCAGCCTGCCA
CAGCCGCTTCCTGCC	CGCGCCGTGTACTGT	CGCCCAGCCTGCCAA
AGCCGCTTCCTGCCT	GCGCCGTGTACTGTC	GCCCAGCCTGCCAAG
GCCGCTTCCTGCCTG	CGCCGTGTACTGTGCG	CCCAGCCTGCCAAGC
35 CCGCTTCCTGCCTGG	GCCGTGTACTGTGCGC	CCAGCCTGCCAAGCA
CGCTTCCTGCCTGGA	CCGTGTACTGTGCGCC	CAGCCTGCCAAGCAG
GCTTCCTGCCTGGAT	CGTGTACTGTGCGCCC	AGCCTGCCAAGCAGC
CTTCCTGCCTGGATT	GTGTACTGTGCGCCCC	GCCTGCCAAGCAGCG
40 TTCCTGCCTGGATTCC	TGTACTGTGCGCCCCA	CCTGCCAAGCAGCGT
TCCTGCCTGGATTCC	GTACTGTGCGCCCCAT	CTGCCAAGCAGCGTG
CCTGCCTGGATTCCA	TACTGTGCGCCCCATC	TGCCAAGCAGCGTGC
CTGCCTGGATTCCAC	ACTGTGCGCCCCATCC	GCCAAGCAGCGTGCC
TGCCTGGATTCCACA	CTGTGCGCCCCATCCC	CCAAGCAGCGTGCCC
GCCTGGATTCCACAG	TGTGCGCCCCATCCCT	CAAGCAGCGTGCCCC
45 CCTGGATTCCACAGC	GTCGCCCCATCCCTG	AAGCAGCGTGCCCCG
CTGGATTCCACAGCT	TCGCCCCATCCCTGC	AGCAGCGTGCCCCGG
TGGATTCCACAGCTT	CGCCCCATCCCTGCG	GCAGCGTGCCCCGGT
GGATTCCACAGCTTC	GCCCCATCCCTGCGC	CAGCGTGCCCCGGTT
GATTCCACAGCTTCG	CCCCATCCCTGCGCG	AGCGTGCCCCGGTTG
50 ATTCCACAGCTTCGCG	CCCATCCCTGCGCGC	GCGTGCCCCGGTTGC
TTCCACAGCTTCGCG	CCATCCCTGCGCGCC	CGTGCCCCGGTTGCA
TCCACAGCTTCGCGC	CATCCCTGCGCGCCC	GTGCCCCGGTTGCAG

TGCCCCGGTTGCAGG
GCCCCGGTTGCAGGC
CCCCGGTTGCAGGCG
CCCGGTTGCAGGCGT
5 CCGGTTGCAGGCGTC
CGGTTGCAGGCGTCA
GGTTGCAGGCGTCAT
GTTGCAGGCGTCATG
TTGCAGGCGTCATGC
10 TGCAGGCGTCATGCA
GCAGGCGTCATGCAG
CAGGCGTCATGCAGC
AGGCGTCATGCAGCG
GGCGTCATGCAGCGG
15 GCGTCATGCAGCGGG
CGTCATGCAGCGGGC
GTCATGCAGCGGGCG
TCATGCAGCGGGCGC
CATGCAGCGGGCGCG
20 ATGCAGCGGGCGCGA
TGCAGCGGGCGCGAC
GCAGCGGGCGCGACC
CAGCGGGCGCGACCC
AGCGGGCGCGACCCA
25 GCGGGCGCGACCCAC
CGGGCGCGACCCACG
GGGCGCGACCCACGC
GGCGCGACCCACGCT
GCGCGACCCACGCTC
30 CGCGACCCACGCTCT
GCGACCCACGCTCTG
CGACCCACGCTCTGG
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35 CCCACGCTCTGGGCC
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CGCTCTGGGCCGCTG
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CTCTGGGCCGCTGCG
TCTGGGCCGCTGCGC
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TGGGCCGCTGCGCTG
45 GGGCCGCTGCGCTGA
GGCCGCTGCGCTGAC
GCCGCTGCGCTGACT
CCGCTGCGCTGACTC
CGCTGCGCTGACTCT
50 GCTGCGCTGACTCTG
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ACTCTGCTGGTGCTG
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CTGCTGGTGCTGCTC
TGCTGGTGCTGCTCC
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GCTCCGCGGGCCGCC
CTCCGCGGGCCGCCG
TCCGCGGGCCGCCGG
CCGCGGGCCGCCGGT
CGCGGGCCGCCGGTG
GCGGGCCGCCGGTGG
CGGGCCGCCGGTGGC
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GGCCGCCGGTGGCGC
CCGCCGGTGGCGCGG
CGCCGGTGGCGCGGG
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GCGAGCTCGGGGGGCT
CGAGCTCGGGGGGCT
GAGCTCGGGGGGCTT
AGCTCGGGGGGCTTG
GCTCGGGGGGCTTGG
CTCGGGGGGCTTGGG
TCGGGGGGCTTGGGT
CGGGGGGCTTGGGT
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GGTGCGCTGCGAGCC
GTGCGCTGCGAGCCG
TGCCTGCGAGCCGT
GCGCTGCGAGCCGTG
CGCTGCGAGCCGTGC
GCTGCGAGCCGTGCG
CTGCGAGCCGTGCGA
TGCGAGCCGTGCGAC
GCGAGCCGTGCGACG
CGAGCCGTGCGACGC
GAGCCGTGCGACGCG
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CGTGCGACGCGCGTG
GTGCGACGCGCGTG
TGCGACGCGCGTGCA
GCGACGCGCGTGCA
CGACGCGCGTGCACT
GACGCGCGTGCACTG
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CGCGCGTGCACTGGC
GCGCGTGCACTGGCC
CGCGTGCACTGGCCC
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CGTGCACTGGCCCA
GTGCACTGGCCCACT
TGCACTGGCCCACTG
GCACTGGCCCACTGC
CACTGGCCCACTGCG
ACTGGCCCACTGCGC
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TGGCCCACTGCGCGC
GGCCCACTGCGCGCC
GCCCACTGCGCGCCT
CCCACTGCGCGCCTC
CCAGTGCGCGCCTCC
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AGTGCGCGCCTCCGC

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- 30 -

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 GTAAATAAAGTTTTT
 TAAATAAAGTTTTTA
 AAATAAAGTTTTTAC
 15 AATAAAGTTTTTACC
 ATAAAGTTTTTACCA
 TAAAGTTTTTACCAT
 AAAGTTTTTACCATT

20

EXAMPLE 8

ANTISENSE OLIGONUCLEOTIDES OF IGF-I RECEPTOR

Antisense oligonucleotides to IGF-I may be selected from molecules capable of interacting with one or more of the following sense oligonucleotides:

25

TTTTTTTTTTTTTTTG	TCATCCCAAATAAAA	GGCTCCGGAGGAGGG
TTTTTTTTTTTTTTGA	CATCCCAAATAAAAG	GCTCCGGAGGAGGGT
TTTTTTTTTTTTTTGAG	ATCCCAAATAAAAGG	CTCCGGAGGAGGGTC
TTTTTTTTTTTTTTGAGA	TCCCAAATAAAAGGA	TCCGGAGGAGGGTCC
30 TTTTTTTTTTTTGAGAA	CCCAAATAAAAGGAA	CCGGAGGAGGGTCCC
TTTTTTTTTTTGAGAAA	CCAAATAAAAGGAAT	CGGAGGAGGGTCCCC
TTTTTTTTTTTGAGAAAG	CAAATAAAAGGAATG	GGAGGAGGGTCCCCG
TTTTTTTTTTTGAGAAAGG	AAATAAAAGGAATGA	GAGGAGGGTCCCCGA
TTTTTTTTTTTGAGAAAGGG	AATAAAAGGAATGAA	AGGAGGGTCCCCGAC
35 TTTTTTGAGAAAGGGA	ATAAAAGGAATGAAG	GGAGGGTCCCCGACC
TTTTTGAGAAAGGGAA	TAAAAGGAATGAAGT	GAGGGTCCCCGACCT
TTTGAGAAAGGGGAAT	AAAAGGAATGAAGTC	AGGGTCCCCGACCTC
TTGAGAAAGGGGAATT	AAAGGAATGAAGTCT	GGGTCCCCGACCTCG
40 TGAGAAAGGGGAATTT	AAGGAATGAAGTCTG	GGTCCCCGACCTCGC
GAGAAAGGGGAATTTT	AGGAATGAAGTCTGG	GTCCCCGACCTCGCT
AGAAAGGGGAATTTCA	GGAATGAAGTCTGGC	TCCCCGACCTCGCTG
GAAAGGGGAATTTTCAT	GAATGAAGTCTGGCT	CCCCGACCTCGCTGT
AAAGGGGAATTTTCATC	AATGAAGTCTGGCTC	CCCGACCTCGCTGTG
AAGGGGAATTTTCATCC	ATGAAGTCTGGCTCC	CCGACCTCGCTGTGG
45 AGGGGAATTTTCATCCC	TGAAGTCTGGCTCCG	CGACCTCGCTGTGGG
GGGAATTTTCATCCCA	GAAGTCTGGCTCCGG	GACCTCGCTGTGGGG
GGAATTTTCATCCCAA	AAGTCTGGCTCCGGA	ACCTCGCTGTGGGGG
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	TGGCTCCGGAGGAGG	GCTGTGGGGGCTCCT

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GAGAAAATCTGCGGGC
AGAAAATCTGCGGGCC
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	GGACCATGGAGGAGA	TACCGCTGCTGGACC	GCGGGCGTGACCCGA
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EXAMPLE 9

INHIBITION OF IGF-I BINDING BY ANTISENSE OLIGONUCLEOTIDES TO IGF-I RECEPTOR

Sub-confluent HaCaT cells were treated as described above with phosphorothioate oligonucleotides IGFR.AS (antisense: 5'-ATCTCTCCGCTTCCTTTC-3'; [SEQ ID NO. 10]; ref 13) and IGFR.S (sense control: 5'-GAAAGGAAGCGGAGAGAT-3'; [SEQ ID NO. 11]; ref 13) IGF-I binding to the cell monolayers was then measured as ¹²⁵I-IGF-I.

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EXAMPLE 10

INHIBITION OF IGFBP-3 PRODUCTION USING ANTISENSE OLIGONUCLEOTIDES

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The results of this experiment are shown in Figures 7 and 8.

HaCaT cells were initially plated in DMEM with 10% v/v serum, then AS oligo experiments were performed in complete "Keratinocyte-SFM" (Gibco) to exclude the influence of exogenous IGFBPs. Oligos were synthesised as phosphorothioate (nuclease-resistant) derivatives (Bresatec, South Australia) and were as follows: antisense: AS2, 5'-GCGCCCGCTGCATGACGCCTGCAAC-3' (IGFBP-3 start codon); controls:

40

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AS2NS, 5'-CGGAGATGCCGCATGCCAGCGCAGG-3'; AS4,
5'-AGGCGGCTGACGGCACTA-3'; AS4NS, 5'-GACAGCGTCGGAGCGATC-3';
IGFRAS, 5'-ATCTCTCCGCTTCCTTTC-3';
IGFRS, 5'-GAAAGGAAGCGGAGAGAT-3'. Oligos to IGFBP-3 were based on the
5 published sequence of Spratt *et al* [12]. AS oligos were added to HaCaT monolayers
in 0.5ml medium in 24-well plates at the concentrations and addition frequencies
indicated. IGFBP-3 measured in cell-conditioned medium using a dot-blot assay,
adapted from the Western ligand blot method of Hossenlopp *et al* [11], in which 100µl
of conditioned medium was applied to nitrocellulose filters with a vacuum dot-blot
10 apparatus. After drying the membranes at 37°C, relative amounts of IGFBP are
determined by ¹²⁵I-IGF-I-binding, autoradiography and computerised imaging
densitometry. Triplicate wells (except in Figure 7, where duplicate wells were measured
as shown) were analysed and corrected for changes in cell number per well. Relative
cell number per well was determined using an amido black dye method, developed
15 specifically for cultured monolayers of HaCaT cells (14). Cell numbers differed by less
than 10% after treatment. For oligos to the IGF receptor, receptor quantitation in intact
HaCaT monolayers was by overnight incubation with ¹²⁵I-IGF-I (30,000cpm/well) at
4°C.

20

EXAMPLE 11

INHIBITION OF IGFBP-2 PRODUCTION USING RIBOZYMES

Experiments involving ribozymes are generally conducted as described in International
Patent Application No. WO 89/05852 and in Haselhoff and Gerlach [8]. Ribozymes are
constructed with a hybridising region which is complementary in nucleotide sequence
25 to at least part of a target RNA which, in this case, encodes IGFBP-2. Activity of
ribozymes is measurable on, for example, Northern blots or using animal models such
as in the nude mouse model (15; 16) or the "flaky skin" mouse model (17; 18).

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EXAMPLE 12**INHIBITION OF IGFBP-3 PRODUCTION USING RIBOZYMES**

The methods described in Example 11 are used for the screening of ribozymes which
5 inhibit IGFBP-3 production. The activity of the ribozymes is determined as in Example
11.

EXAMPLE 13**INHIBITION OF IGF-1 PRODUCTION USING RIBOZYMES**

10 The methods described in Example 11 are used for the screening of ribozymes which
inhibit IGF-1 production. The activity of the ribozymes is determined as in Example
11.

EXAMPLE 14

15 **INHIBITION OF IGF-1 RECEPTOR PRODUCTION USING RIBOZYMES**

The methods described in Example 11 are used for the screening of ribozymes which
inhibit IGF-1 production. The activity of the ribozymes is determined as in Example
11.

20 Those skilled in the art will appreciate that the invention described herein is susceptible
to variations and modifications other than those specifically described. It is to be
understood that the invention includes all such variations and modifications. The
invention also includes all of the steps, features, compositions and compounds referred
to or indicated in this specification, individually or collectively, and any and all
25 combinations of any two or more of said steps or features.

REFERENCES:

1. Sara V *Physiological Reviews* **70**: 591-614, 1990.
2. Rechler MM and Brown AL *Growth Regulation* **2**: 55-68, 1992.
3. Clemmons DR *Growth Regn* **2**: 80, 1992.
4. Oakes SR, KM Haynes, MJ Waters, AC Herington and GA Werther *J. Clin Endocrinol Metab* **73**: 1368-1373, 1992.
5. Camacho-Hubner C *et al.* *J Biol Chem* **267**: 11949-11956, 1992.
6. Neely KE *et al.* *J Inv Derm* **96**: 104, 1991.
7. Ts'O POP, Aurelian L, Chang E and Miller PS. Nonionic oligonucleotide analogs (Matagen TM) as anticodic agents in duplex and triplex formation. in "Antisense Strategies", Annals of the New York Academy of Sciences **660**:159-177 (Baserga R and Denhardt DT, eds.), 1993.
8. Haseloff J and Gerlach L *Nature* **334**: 586-591, 1988.
9. Boukamp P, Petrussevska RT, Breitkreuz D, Hornung J, Markham A, Fusenig NE. *J Cell Biol* **106**: 761-771, 1988.
10. Rheinwald and Green *Cell* **6**: 331-344, 1975.
11. Hossenlopp P, Seurin D, Segovia-Quinson B, Hardouin S, Binoux M. *Anal Biochem* **154**: 138-143, 1986.

12. Spratt SK, Tatsuno GP, Yamanaka MK, Ark BC, Detmer J, Mascarenhas D, Flynn J, Talkington-Verser C, Spencer EM. *Growth Factors* 3: 63-72, 1990.
13. Pietrzkowski, Z, Sell C, Lammers R, Ullrich A and Baserga R. *Mol. Cell. Biol.* 12: 3883-3889, 1992.
14. Schulz J, Dettlaff S, Fritzsche U, Harms U, Schiebel H, Derer W, Fusenig NE, Hulsen A and Bohm M. *J. Immunol. Meth.* 167: 1-13, 1994.
15. Baker BS, Brent L, Valdimarsson H, Powles AV, Al-Imara L, Walker M and Fry L. *Brit. J. Dermatol* 126: 105-110, 1992.
16. Nanney LB et al *J. Invest. Dermatol* 98: 296-301, 1992.
17. Sundberg JP et al *Immunol. Investigations* 22: 389-401, 1993.
18. Sundberg JP et al *J. Invest. Dermatol* 102: 781-788, 1994.

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SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT (countries other than US): ROYAL CHILDREN'S HOSPITAL
RESEARCH FOUNDATION
(US only): George A WERTHER and Christopher J WRAIGHT
- (ii) TITLE OF INVENTION: A METHOD FOR THE PROPHYLAXIS
AND/OR TREATMENT OF PROLIFERATIVE
AND/OR INFLAMMATORY SKIN DISORDERS
- (iii) NUMBER OF SEQUENCES: 11
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: DAVIES COLLISON CAVE
 - (B) STREET: 1 LITTLE COLLINS STREET
 - (C) CITY: MELBOURNE
 - (D) STATE: VICTORIA
 - (E) COUNTRY: AUSTRALIA
 - (F) ZIP: 3000
- (v) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
- (vi) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER: PCT INTERNATIONAL
 - (B) FILING DATE: 06-JUL-1995
- (vii) PRIOR APPLICATION DATA:
 - (A) APPLICATION NUMBER: PM6725/94
 - (B) FILING DATE: 08-JUL-1994
- (viii) ATTORNEY/AGENT INFORMATION:
 - (A) NAME: HUGHES, Dr E JOHN L
 - (C) REFERENCE/DOCKET NUMBER: EJH/EK
- (ix) TELECOMMUNICATION INFORMATION:
 - (A) TELEPHONE: +61 3 9254 2777
 - (B) TELEFAX: +61 3 9254 2770

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(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1433 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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AAGCCCCTCA AGTCGGGTAT GAAGGAGCTG GCCGTGTTCC GGGAGAAGGT CACTGAGCAG      720
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CCCAACTGTG ACAAGCATGG CCTGTACAAC CTCAAACAGT GCAAGATGTC TCTGAACGGG      960
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(2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2474 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

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GGCGCGGGCT GGCGCGAGCT CGGGGGGCTT GGGTCCCGTG GTGCGCTGCG AGCCGTGCGA   240
CGCGCGTGCA CTGGCCCAGT GCGCGCCTCC GCCCGCCGTG TCGCGGAGC TGGTGC GCGA   300
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(2) INFORMATION FOR SEQ ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4989 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

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GAGTTTCTCA ACGAAGCTTC TGTGATGAAG GAGTTCAATT GTCACCATGT GGTGCGATTG 3240

- 82 -

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- 83 -

(2) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

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25

(2) INFORMATION FOR SEQ ID NO:5:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

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24

(2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 18 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

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18

(2) INFORMATION FOR SEQ ID NO:7:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 19 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CAGGCGTCAT GCAGCGGGC

19

- 84 -

(2) INFORMATION FOR SEQ ID NO:8:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

CGGAGATGCC GCATGCCAGC GCAGG

25

(2) INFORMATION FOR SEQ ID NO:9:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 18 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

GACAGCGTCG GAGCGATC

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(2) INFORMATION FOR SEQ ID NO:10:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 18 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

ATCTCTCCGC TTCCTTTC

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(2) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 18 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

GAAAGGAAGC GGAGAGAT

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CLAIMS:

1. A method for ameliorating the effects of a proliferative and/or inflammatory skin disorder in a mammal, said method comprising contacting the proliferating and/or inflamed skin or skin capable of proliferation and/or inflammation with an effective amount of a nucleic acid molecule or chemical analogue thereof capable of inhibiting or otherwise reducing growth factor mediated cell proliferation and/or inflammation.
2. A method according to claim 1 wherein cell proliferation and/or inflammation is mediated by at least one of insulin-like growth factor I (IGF-I), keratinocyte growth factor (KGF), transforming growth factor- α (TGF α), tumour necrosis factor- α (TNF α), interleukin (IL) -1 (IL-1), IL-4, IL-6, IL-8 and/or basic fibroblast growth factor (bFGF).
3. A method according to claim 2 wherein cell proliferation and/or inflammation is mediated by IGF-I.
4. A method according to claim 1 wherein the nucleic acid molecule inhibits or otherwise reduces IGF-I mediated cell proliferation and/or inflammation.
5. A method according to claim 1 wherein the proliferative or inflammatory skin disorder is psoriasis, ichthyosis, pityriasis, rubra, pilaris, seborrhoea, keloids, keratosis, neoplasias, scleroderma, warts, benign growths or cancers of the skin.
6. A method according to claim 5 wherein the skin condition is psoriasis.
7. A method according to claim 1 or 4 or 6 wherein the mammal is a human.
8. A method according to claim 1 or 4 or 6 wherein the nucleic acid molecule is capable of inhibiting, reducing or otherwise interfering with IGF-I-interaction with its receptor.

9. A method according to claim 8 wherein the nucleic acid molecule is an antisense molecule capable of reducing expression of a gene encoding IGF-I, IGF-I-receptor or an IGF binding protein (IGFBP).

10. A method according to claim 9 wherein the nucleic acid molecule is an antisense molecule capable of reducing expression of a gene encoding IGFBP-2, -3, -4, -5 or -6.

11. A method according to claim 10 wherein the nucleic acid molecule is an antisense molecule capable of reducing expression of a gene encoding IGFBP-2 or IGFBP-3.

12. A method according to claim 11 wherein the antisense molecule is at least about 15 nucleotides in length and is capable of interacting with at least one sequence selected from the list set forth in Example 6 or Example 7.

13. A method according to claim 11 wherein the antisense molecule comprises the nucleotide sequence:

5'-ATCTCTCCGCTTCCTTTC-3' [SEQ ID NO:10].

14. A nucleic acid molecule comprising at least about 10 nucleotides capable of hybridising to or forming a heteroduplex or otherwise interacting with an RNA molecule directed from a gene corresponding to a genomic form of SEQ ID NO:1 and/or SEQ ID NO:2 and which thereby reduces or inhibits translation of said RNA molecule.

15. A nucleic acid molecule according to claim 14 wherein said molecule comprises at least about 15 nucleotides.

16. A nucleic acid molecule according to claim 15 wherein said molecule is capable of interacting with at least one nucleotide sequence selected from the list set forth in Example 6 and Example 7.

17. A nucleic acid molecule according to claim 15 or 16 comprising the nucleotide sequence:

5'-ATCTCTCCGCTTCCTTTC-3' [SEQ ID NO:10].

18. A method of ameliorating the effects of psoriasis, said method comprising contacting proliferating skin or skin capable of proliferation with an effective amount of one or more nucleic acid molecules or chemical analogues thereof capable of inhibiting or otherwise reducing IGF-I mediated cell proliferation wherein said one or more molecules comprises a polynucleotide capable of interacting with mRNA directed from an IGF-I gene, an IGF-I receptor gene or a gene encoding an IGFBP.

19. A method according to claim 18 wherein the IGFBP is IGFBP-2 or IGFBP-3.

20. A method according to claim 18 or 19 wherein the mammal is a human.

21. A method according to claim 20 wherein the nucleic acid molecule is capable of interacting with a nucleotide sequence selected from the list set forth in Example 6 or Example 7.

22. A method according to claim 18 wherein the nucleic acid molecule comprises the nucleotide sequence:

5'-ATCTCTCCGCTTCCTTTC-3' [SEQ ID NO:10].

23. A pharmaceutical composition for topical administration said composition comprising a nucleic acid molecule capable of inhibiting or otherwise reducing IGF-I mediated cell proliferation said composition further comprising one or more pharmaceutically acceptable carriers and/or diluents.

24. A pharmaceutical composition according to claim 23 wherein the nucleic acid molecule is an antisense molecule to a gene encoding IGF-I, IGF-I-receptor or an IGFBP.

25. A pharmaceutical composition according to claim 24 wherein the nucleic acid molecule is capable of targeting a gene encoding IGFBP-2 and/or IGFBP-3.
26. A pharmaceutical composition according to claim 24 capable of interacting with at least one nucleotide sequence set forth in Example 6 or Example 7.
27. Use of a nucleic acid molecule in the manufacture of a medicament for the treatment of a proliferative and/or inflammatory skin disorder mediated by IGF-I.
28. Use according to claim 27 wherein the skin disorder is psoriasis.
29. A ribozyme comprising a hybridising region and a catalytic region wherein the hybridising region is capable of hybridising to at least part of a target mRNA sequence transcribed from a genomic gene corresponding to SEQ ID NO:1 or SEQ ID NO:2 wherein said catalytic domain is capable of cleaving said target mRNA sequence to reduce or inhibit IGF-I mediated cell proliferation or inflammation.

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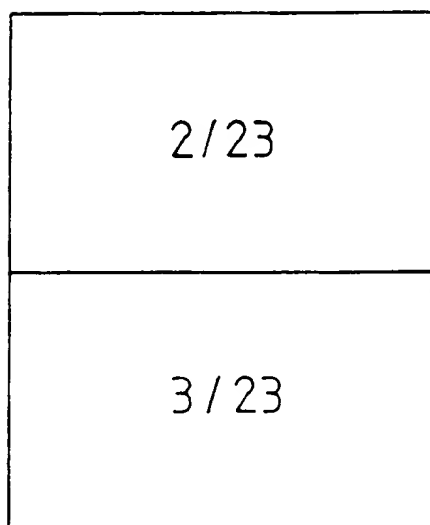


FIG 1

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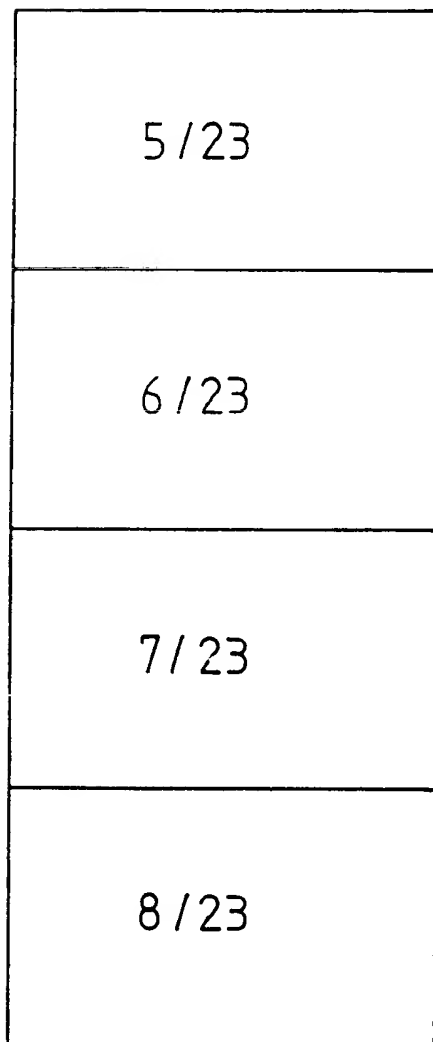
FIGURE 1

1	ATTCGGGGCG	AGGGAGGAGG	AAGAAGCGGA	GGAGGCGGGCT	CCCGCTCGCA
51	GGGCCGTGCA	CCTGCCCGCC	CGCCCGCTCG	CTCGCTCGCC	CGCCGCGCCG
101	CGCTGCCGAC	CGCCAGCATG	CTGCCGAGAG	TGGGCTGCCC	CGCGCTGCCG
151	CTGCCGCCGC	CGCCGCTGCT	GCCGCTGCTG	CCGCTGCTGC	TGCTGCTACT
201	GGGCGCGAGT	GGCGGCGGCG	GCGGGGCGCG	CGCGGAGGTG	CTGTTCCGCT
251	GCCCGCCCTG	CACACCCGAG	CGCCTGGCCG	CCTGCGGGCC	CCCGCCGGTT
301	GCGCCGCCCG	CCGCGGTGGC	CGCAGTGGCC	GGAGGCGCCC	GCATGCCATG
351	CGCGGAGCTC	GTCCGGGAGC	CGGGCTGCGG	CTGCTGCTCG	GTGTGCGCCC
401	GGCTGGAGGG	CGAGGCGTGC	GGCGTCTACA	CCCCGCGCTG	CGGCCAGGGG
451	CTGCGCTGCT	ATCCCCACCC	GGGCTCCGAG	CTGCCCCCTGC	AGGCGCTGGT
501	CATGGGCGAG	GGCACTTGTTG	AGAAGCGCCG	GGACGCCGAG	TATGGCGCCA
551	GCCCGGAGCA	GGTTGCAGAC	AATGGCGATG	ACCACTCAGA	AGGAGGCCCTG
601	GTGGAGAACC	ACGTGGACAG	CACCATGAAC	ATGTTGGGCG	GGGGAGGCAG
651	TGCTGGCCCG	AAGCCCCCTCA	AGTCGGGTAT	GAAGGAGCTG	GCCGTGTTCC
701	GGGAGAAGGT	CACTGAGCAG	CACCGGCAGA	TGGGCAAGGG	TGGCAAGCAT

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FIGURE 1 (continued...)

751	CACCTTGGCC	TGGAGGAGCC	CAAGAAGCTG	CGACCACCCC	CTGCCAGGAC
801	TCCCTGCCAA	CAGGAACTGG	ACCAGGTCCT	GGAGCGGATC	TCCACCATGC
851	GCCTTCCGGA	TGAGCGGGC	CCTCTGGAGC	ACCTCTACTC	CCTGCACATC
901	CCCAACTGTG	ACAAGCATGG	CCTGTACAAC	CTCAAACAGT	GCAAGATGTC
951	TCTGAACGGG	CAGCGTGGG	AGTGCTGGTG	TGTGAACCCC	AACACCGGGA
1001	AGCTGATCCA	GGAGCCCCC	ACCATCCGGG	GGGACCCCGA	GTGTCATCTC
1051	TTCTACAATG	AGCAGCAGGA	GGCTTGCGGG	GTGCACACCC	AGCGGATGCA
1101	GTAGACCGCA	GCCAGCCGGT	GCCTGGCGCC	CCTGCCCCCC	GCCCCCTCTCC
1151	AAACACCGGC	AGAAACGGA	GAGTGCTTGG	GTGGTGGGTG	CTGGAGGATT
1201	TTCCAGTTCT	GACACACGTA	TTTATATTG	GAAAGAGACC	AGCACCGAGC
1251	TCGGCACCTC	CCCGGCCCTCT	CTCTTCCCAG	CTGCAGATGC	CACACCTGCT
1301	CCTTCTTGCT	TTCCCCGGGG	GAGGAAGGGG	GTTGTGGTCG	GGGAGCTGGG
1351	GTACAGGTTT	GGGAGGGGG	AAGAGAAATT	TTTATTTTGG	AACCCCTGTG
1401	TCCCTTTTGC	ATAAGATTAA	AGGAAGGAAA	AGT	

$4/23$ FIG 2

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FIGURE 2

1	CTCAGCGCCC	AGCCGCTTCC	TGCCCTGGATT	CCACAGCTTC	GCGCCGTGTA
51	CTGTGCCCC	ATCCCTGCGC	GCCCAGCCTG	CCAAGCAGCG	TGCCCCGGTT
101	GCAGGCGTCA	TGCAGCGGGC	GCGACCCACG	CTCTGGGCCG	CTGCGCTGAC
151	TCTGCTGGTG	CTGCTCCGCG	GGCCGCCCGT	GGCGCGGGCT	GGCGGAGCT
201	CGGGGGGCTT	GGGTCCCGTG	GTGCGCTGCG	AGCCGTGCGA	CGCGCGTGCA
251	CTGGCCCAGT	GCGCGCCTCC	GCCCGCCGTG	TGCGCGGAGC	TGGTGCGCGA
301	GCCGGGCTGC	GGCTGCTGCC	TGACGTGCGC	ACTGAGCGAG	GGCCAGCCGT
351	GCGGCATCTA	CACCGAGCGC	TGTGGCTCCG	GCC TTCGTG	CCAGCCGTCG
401	CCCGACGAGG	CGCGACCGCT	GCAGGCGCTG	CTGGACGGCC	GCGGGCTCTG
451	CGTCAACGCT	AGTGCCCGTCA	GCCGCCCTGCG	CGCCTACCTG	CTGCCAGCGC
501	CGCCAGCTCC	AGGAAATGCT	AGTGAGTCGG	AGGAAGACCG	CAGCGCCGGC
551	AGTGTGGAGA	GCCCGTCCGT	CTCCAGCACG	CACCGGGTGT	CTGATCCCAA
601	GTTCCACCCC	CTCCATTCAA	AGATAATCAT	CATCAAGAAA	GGGCATGCTA
651	AAGACAGCCA	GCGCTACAAA	GTTGACTACG	AGTCTCAGAG	CACAGATACC
701	CAGAACTTCT	CCTCCGAGTC	CAAGCGGGAG	ACAGAATATG	GTCCCTGCCG

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FIGURE 2 (Continued...)

751	TAGAGAAATG	GAAGACACAC	TGAATCACCT	GAAGTTCCTC	AATGTGCTGA
801	GTCCCAGGG	TGTACACATT	CCCAACTGTG	ACAAGAAGG	ATTTATAAG
851	AAAAAGCAGT	GTCGCCCTTC	CAAAGGCAGG	AAGCGGGGCT	TCTGCTGGTG
901	TGTGGATAAG	TATGGGCAGC	CTCTCCCAGG	CTACACCACC	AAGGGGAAGG
951	AGGACGTGCA	CTGCTACAGC	ATGCAGAGCA	AGTAGACGCC	TGCCGCAAGT
1001	TAATGTGGAG	CTCAAAATATG	CCTTATTTTG	CACAAAAGAC	TGCCAAGGAC
1051	ATGACCAGCA	GCTGGCTACA	GCCTCGATT	ATATTTCTGT	TTGTGGTGAA
1101	CTGATTTTTT	TTAAACCAAA	GTTTAGAAAG	AGGTTTTTGA	AATGCCCTATG
1151	GTTTCTTTGA	ATGGTAAACT	TGAGCATCTT	TTCACTTTCC	AGTAGTCAGC
1201	AAAGAGCAGT	TTGAATTTTC	TTGTCGCTTC	CTATCAAAAT	ATTCAGAGAC
1251	TCGAGCACAG	CACCCAGACT	TCATGCGCCC	GTGGAATGCT	CACCACATGT
1301	TGGTCGAAGC	GGCCGACCAC	TGACTTTGTG	ACTTAGGCGG	CTGTGTTGCC
1351	TATGTAGAGA	ACACGCTTCA	CCCCCACTCC	CCGTACAGTG	CGCACAGGCT
1401	TTATCGAGAA	TAGGAAAACC	TTTAAACCCC	GGTCATCCGG	ACATCCCAAC
1451	GCATGCTCCT	GGAGCTCACA	GCCTTCTGTG	GTGTCAATTTC	TGAAACAAGG

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FIGURE 2 (Continued...)

1501	GCGTGGATCC	CTCAACCAAG	AAGAATGTTT	ATGTCTTCAA	GTGACCTGTA
1551	CTGCTTGGGG	ACTATTGGAG	AAAATAAGGT	GGAGTCCTAC	TTGTTTAAAA
1601	AATATGTATC	TAAGAAATGT	CTAGGGCACT	CTGGGAACCT	ATAAAGGCAG
1651	GTATTTTCGG	CCCTCCTCTT	CAGGAATCTT	CCTGAAGACA	TGGCCAGTC
1701	GAAGGCCCCAG	GATGGCTTTT	GCTGCCGGCC	CGTGGGGTAG	GAGGGACAGA
1751	GAGACGGGAG	AGTCAGCCTC	CACATTCAGA	GGCATCACAA	GTAATGGCAC
1801	AATTCTTCGG	ATGACTGCAG	AAAATAGTGT	TTTGTAGTTC	AACAACCTCAA
1851	GACGAAGCTT	ATTTCTGAGG	ATAAGCTCTT	TAAAGGCAAA	GCTTTATTTT
1901	CATCTCTCAT	CTTTTGTCTT	CCTTAGCACA	ATGTAAAAAA	GAATAGTAAT
1951	ATCAGAACAG	GAAGGAGGAA	TGGCTTGCTG	GGGAGCCCAT	CCAGGACACT
2001	GGGAGCACAT	AGAGATTAC	CCATGTTTGT	TGAACTTAGA	GTCATTCTCA
2051	TGCTTTTCTT	TATAATTCAC	ACATATATGC	AGAGAAGATA	TGTTCTTGTT
2101	AACATTGTAT	ACAACATAGC	CCCAATATA	GTAAGATCTA	TACTAGATAA
2151	TCCTAGATGA	AATGTTAGAG	ATGCTATATG	ATACAACTGT	GGCCATGACT
2201	GAGGAAAGGA	GCTCACGCCC	AGAGACTGGG	CTGCTCTCCC	GGAGGCCAAA

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FIGURE 2 (Continued...)

2251	CCCAAGAAGG	TCTGGCAAAG	TCAGGCTCAG	GGAGACTCTG	CCCTGCTGCA
2301	GACCTCGGTG	TGGACACACG	CTGCATAGAG	CTCTCCTTGA	AAACAGAGGG
2351	GTCTCAAGAC	ATTCTGCCCTA	CCTATTAGCT	TTTCTTTTAT	TTTTTAACTT
2401	TTTGGGGGGA	AAAGTATTTT	TGAGAAAGTTT	GTCTTGCAAT	GTATTTATAA
2451	ATAGTAAATA	AAGTTTTTAC	CATT		

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FIG 3

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FIGURE 3

1	TTTTTTTTTT	TTTTGAGAAA	GGGAATTTC	TCCCAAATAA	AAGGAATGAA
51	GTCTGGCTCC	GGAGGAGGGT	CCCCGACCTC	GCTGTGGGGG	CTCCTGTTTC
101	TCTCCGCCGC	GCTCTCGCTC	TGGCCGACGA	GTGGAGAAAT	CTGCCGGCCA
151	GGCATCGACA	TCCGCAACGA	CTATCAGCAG	CTGAAGCGCC	TGGAGAACTG
201	CACGGTGATC	GAGGGCTACC	TCCACATCCT	GCTCATCTCC	AAGGCCGAGG
251	ACTACCGCAG	CTACCGCTTC	CCCAAGCTCA	CGGTCATTAC	CGAGTACTTG
301	CTGCTGTTCC	GAGTGGCTGG	CCTCGAGAGC	CTCGGAGACC	TCTTCCCCAA
351	CCTCACGGTC	ATCCGCGGCT	GAAACTCTT	CTACAACCTAC	GCCCTGGTCA
401	TCTTCGAGAT	GACCAATCTC	AAGGATATTG	GGCTTTACAA	CCTGAGGAAC
451	ATTACTCGGG	GGGCCATCAG	GATTGAGAAA	AATGCTGACC	TCTGTTACCT
501	CTCCACTGTG	GACTGGTCCC	TGATCCTGGA	TGCGGTGTCC	AATAACTACA
551	TTGTGGGGAA	TAAGCCCCCA	AAGGAATGTG	GGGACCTGTG	TCCAGGGACC
601	ATGGAGGAGA	AGCCGATGTG	TGAGAAGACC	ACCATCAACA	ATGAGTACAA
651	CTACCGCTGC	TGGACCACAA	ACCGCTGCCA	GAAAATGTGC	CCAAGCACGT
701	GTGGGAAGCG	GGCGTGCACC	GAGAACAAATG	AGTGCTGCCA	CCCCGAGTGC

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FIGURE 3 (Continued...)

751	CTGGGCAGCT	GCAGCGCGCC	TGACAAACGAC	ACGGCCTGTG	TAGCTTGCCG
801	CCACTACTAC	TATGCCGGTG	TCTGTGTGCC	TGCCCTGCCCG	CCCAACACCT
851	ACAGGTTTGA	GGGCTGGCGC	TGTGTGGACC	GTGACTTCTG	CGCCAACATC
901	CTCAGCGCCG	AGAGCAGCGA	CTCCGAGGGG	TTTGTGATCC	ACGACGGCGA
951	GTGCATGCAG	GAGTGCCCT	CGGGCTTCAT	CCGCAACGGC	AGCCAGAGCA
1001	TGTA CTGCAT	CCCTTGTGAA	GGTCCTTGCC	CGAAGGTCTG	TGAGGAAGAA
1051	AAGAAAACAA	AGACCATTGA	TTCTGTTACT	TCTGCTCAGA	TGCTCCAAGG
1101	ATGCACCATC	TTCAAGGGCA	ATTTGCTCAT	TAACATCCGA	CGGGGAATA
1151	ACATTGCTTC	AGAGCTGGAG	AAC TTCATGG	GGCTCATCGA	GGTGGTGACG
1201	GGCTACGTGA	AGATCCGCCA	TTCTCATGCC	TTGGTCTCCT	TGTCCTTCCT
1251	AAAAAACCTT	CGCCTCATCC	TAGGAGAGGA	GCAGCTAGAA	GGGAATTACT
1301	CCTTCTACGT	CCTCGACAAC	CAGAACTTGC	AGCAACTGTG	GGACTGGGAC
1351	CACCGCAACC	TGACCATCAA	AGCAGGGAAA	ATGTACTTTG	CTTTCATCC
1401	CAAATTATGT	GTTTCCGAAA	TTTACC GCAT	GGAGGAAGTG	ACGGGACTA
1451	AAGGGCGCCA	AAGCAAAGGG	GACATAAACA	CCAGGAACAA	CGGGGAGAGA

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FIGURE 3 (Continued...)

1501	GCCTCCTGTG	AAAGTGACGT	CCTGCATTTC	ACCTCCACCA	CCACGTCGAA
1551	GAATCGCATC	ATCATAACCT	GGCACCGGTA	CCGGCCCCCT	GACTACAGGG
1601	ATCTCATCAG	CTTCACCGTT	TACTACAAGG	AAGCACCCCTT	TAAGAAATGTC
1651	ACAGAGTATG	ATGGGCAGGA	TGCCTGCGGC	TCCAACAGCT	GGAACATGGT
1701	GGACGTGGAC	CTCCCGCCCA	ACAAGGACGT	GGAGCCCGGC	ATCTTACTAC
1751	ATGGGCTGAA	GCCCTGGACT	CAGTACGCCG	TTTACGTCAA	GGCTGTGACC
1801	CTCACCATGG	TGGAGAACGA	CCATATCCGT	GGGGCCAAGA	GTGAGATCTT
1851	GTACATTTCG	ACCAATGCTT	CAGTTCCTTC	CATTCCCTTG	GACGTTCTTT
1901	CAGCATCGAA	CTCCTCTTCT	CAGTTAATCG	TGAAGTGGAA	CCCTCCCTCT
1951	CTGCCCCAACG	GCAACCTGAG	TTACTACATT	GTGCGCTGGC	AGCGGCAGCC
2001	TCAGGACGGC	TACCTTTACC	GGCACAATTA	CTGCTCCAAA	GACAAAATCC
2051	CCATCAGGAA	GTATGCCCGAC	GGCACCATCG	ACATTGAGGA	GGTCACAGAG
2101	AACCCCAAGA	CTGAGGTGTG	TGGTGCGGAG	AAAGGGCCTT	GCTGCGCCTG
2151	CCCCAAAAC	GAAGCCGAGA	AGCAGGCCGA	GAAGGAGGAG	GCTGAATACC
2201	GCAAAGTCTT	TGAGAAATTTC	CTGCACAACT	CCATCTTCGT	GCCCAGACCT

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FIGURE 3 (Continued...)

2251	GAAAGGAAGC	GGAGAGATGT	CATGCAAGTG	GCCAACACCA	CCATGTCCAG
2301	CCGAAGCAGG	AACACCCACGG	CCGCAGACAC	CTACAACATC	ACCGACCCCG
2351	AAGAGCTGGA	GACAGAGTAC	CCTTTCTTTG	AGAGCAGAGT	GGATAACAAG
2401	GAGAGAACTG	TCATTTCTAA	CCTTCGGCCT	TTCACATTGT	ACCGCATCGA
2451	TATCCACAGC	TGCAACCACG	AGGCTGAGAA	GCTGGGCTGC	AGCGCCTCCA
2501	ACTTCGTCTT	TGCAAGGACT	ATGCCCCGAG	AAGGAGCAGA	TGACATTCCCT
2551	GGGCCAGTGA	CCTGGGAGCC	AAGGCCCTGAA	AACCTCCATCT	TTTAAAGTG
2601	GCCGGAACCT	GAGAATCCCA	ATGGATTGAT	TCTAATGTAT	GAAATAAAAT
2651	ACGGATCACA	AGTTGAGGAT	CAGCGAGAAT	GTGTGTCCAG	ACAGGAATAC
2701	AGGAAGTATG	GAGGGGCCAA	GCTAAACCCG	CTAAACCCCG	GGAACTACAC
2751	AGCCCGGATT	CAGGCCACAT	CTCTCTCTGG	GAATGGGTCG	TGGACAGATC
2801	CTGTGTTCTT	CTATGTCCAG	GCCAAAACAG	GATATGAAA	CTTCATCCAT
2851	CTGATCATCG	CTCTGCCCCGT	CGCTGTCCCTG	TTGATCGTGG	GAGGGTTGGT
2901	GATTATGCTG	TACGTCTTCC	ATAGAAAGAG	AAATAACAGC	AGGCTGGGGA
2951	ATGGAGTGCT	GTATGCCCTCT	GTGAACCCCG	AGTACTTCAG	CGCTGCTGAT

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FIGURE 3 (Continued...)

3001	GTGTACGTTC	CTGATGAGTG	GGAGGTGGCT	CGGAGAAGA	TCACCATGAG
3051	CCGGGAACCTT	GGGCAGGGGT	CGTTTGGGAT	GGTCTATGAA	GGAGTTGCCA
3101	AGGGTGTGGT	GAAAGATGAA	CCTGAAACCA	GAGTGGCCAT	TAAACAGTG
3151	AACGAGGCCG	CAAGCATGCG	TGAGAGGATT	GAGTTTCTCA	ACGAAGCTTC
3201	TGTGATGAAG	GAGTTCAATT	GTCACCATGT	GGTGCGATTG	CTGGGTGTGG
3251	TGTCCCAAGG	CCAGCCAACA	CTGGTCATCA	TGGAAC TGAT	GACACGGGGC
3301	GATCTCAAAA	GTTATCTCCG	GTCTCTGAGG	CCAGAAATGG	AGAATAATCC
3351	AGTCCTAGCA	CCTCCAAGCC	TGAGCAAGAT	GATTCAGATG	GCCGGAGAGA
3401	TTGCAGACGG	CATGGCATA	CTCAACGCCA	ATAAGTTCGT	CCACAGAGAC
3451	CTTGCTGCCC	GGAATTGCAT	GGTAGCCGAA	GATTTCACAG	TCAAAATCGG
3501	AGATTTTGGT	ATGACGCGAG	ATATCTATGA	GACAGACTAT	TACCGGAAAG
3551	GAGGCAAAGG	GCTGCTGCCC	GTGCGCTGGA	TGTCTCCTGA	GTCCCTCAAG
3601	GATGGAGTCT	TCACCACTTA	CTCGGACGTC	TGGTCCCTTCG	GGGTCTCTCT
3651	CTGGGAGATC	GCCACACTGG	CCGAGCAGCC	CTACCAGGGC	TTGTCCAACG
3701	AGCAAGTCCT	TCGCTTTCGTC	ATGGAGGGCG	GCCTTCTGGA	CAAGCCAGAC

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FIGURE 3 (Continued...)

3751	AACTGTCCCTG	ACATGCTGTT	TGAACTGATG	CGCATGTGCT	GGCAGTATAA
3801	CCCCAAGATG	AGGCCTTCCT	TCCTGGAGAT	CATCAGCAGC	ATCAAAGAGG
3851	AGATGGAGCC	TGGCTTCCGG	GAGGTCTCCT	TCTACTACAG	CGAGGAGAAC
3901	AAGCTGCCCG	AGCCGGAGGA	GCTGGACCTG	GAGCCAGAGA	ACATGGAGAG
3951	CGTCCCCCTG	GACCCCTCGG	CCTCCTCGTC	CTCCCTGCCA	CTGCCCGACA
4001	GACACTCAGG	ACACAAGGCC	GAGAACGGCC	CCGGCCCTGG	GGTGCTGGTC
4051	CTCCGCGCCA	GCTTCGACGA	GAGACAGCCT	TACGCCCCACA	TGAACGGGGG
4101	CCGCAAGAAC	GAGCGGGCCT	TGCCGCTGCC	CCAGTCTTCG	ACCTGCTGAT
4151	CCTTGATCC	TGAATCTGTG	CAAACAGTAA	CGTGTGCGCA	CGCGCAGCGG
4201	GGTGGGGGGG	GAGAGAGAGT	TTTAACAATC	CATTCACAAG	CCTCCTGTAC
4251	CTCAGTGGAT	CTTCAGTTCT	GCCCTTGCTG	CCCGCGGGAG	ACAGCTTCTC
4301	TGCAGTAAAA	CACATTGGG	ATGTTCCTTT	TTTCAATATG	CAAGCAGCTT
4351	TTTATTCCCT	GCCCAAACCC	TTAACTGACA	TGGGCCTTTA	AGAACCTTAA
4401	TGACAACACT	TAATAGCAAC	AGAGCACTTG	AGAACCAGTC	TCCTCACTCT
4451	GTCCCTGTCC	TTCCCTGTTC	TCCCTTTCTC	TCTCCTCTCT	GCTTCATAAC

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FIGURE 3 (Continued...)

4501	GGAAAAATAA	TTGCCACAAG	TCCAGCTGGG	AAGCCCTTTT	TATCAGTTTG
4551	AGGAAGTGGC	TGTCCCTGTG	GCCCCATCCA	ACCACTGTAC	ACACCCGCCCT
4601	GACACCGTGG	GTCAATTACAA	AAAAACACGT	GGAGATGGAA	ATTTTTACCT
4651	TTATCTTTCA	CCTTTCTAGG	GACATGAAAT	TTACAAAGGG	CCATCGTTCA
4701	TCCAAGGCTG	TTACCAATTT	AACGCTGCCT	AATTTGCCA	AAATCCTGAA
4751	CTTTCTCCCT	CATCGGCCCG	GCGCTGATTC	CTCGTGTCGG	GAGGCATGGG
4801	TGAGCATGGC	AGCTGGTTGC	TCCATTTGAG	AGACACGCTG	GCGACACACT
4851	CCGTCCATCC	GACTGCCCCCT	GCTGTGCTGC	TCAAGGCCAC	AGGCACACAG
4901	GTCTCATTGC	TTCTGACTAG	ATTATTATT	GGGGGAACTG	GACACAATAG
4951	GTCTTTCTCT	CAGTGAAGGT	GGGGAGAAGC	TGAACCGGC	

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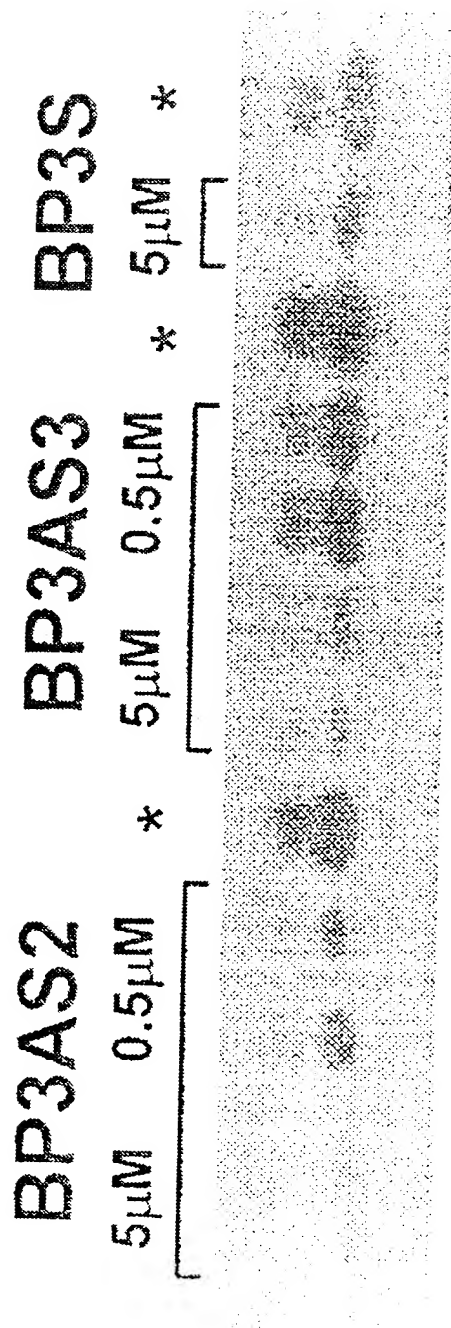


FIG 4A

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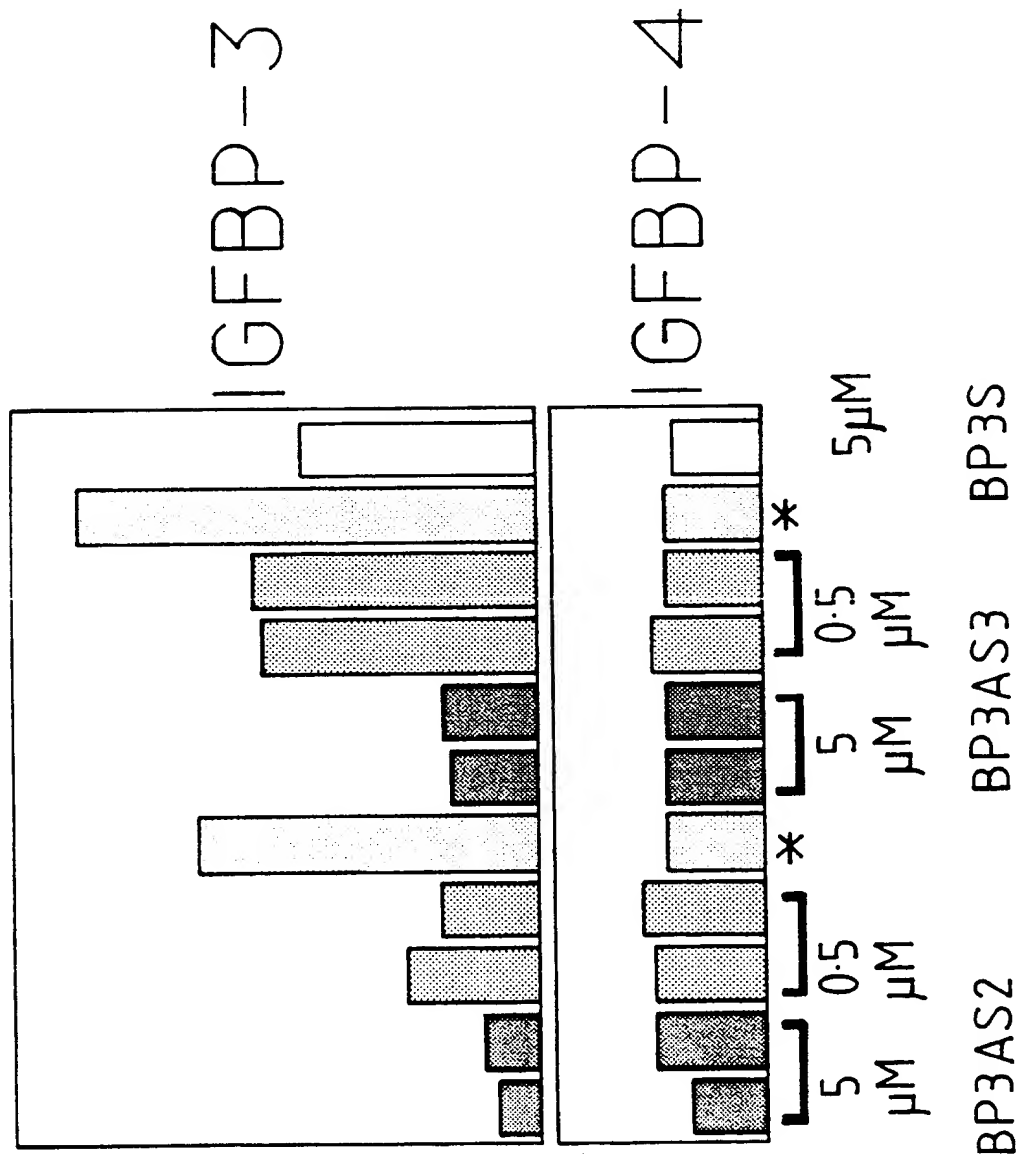


FIG 4B

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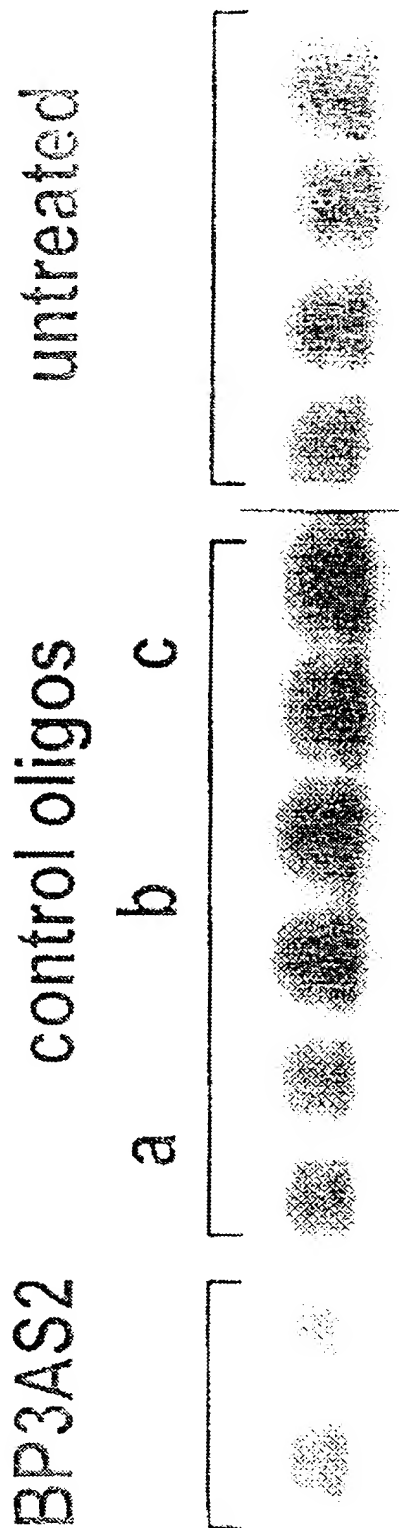
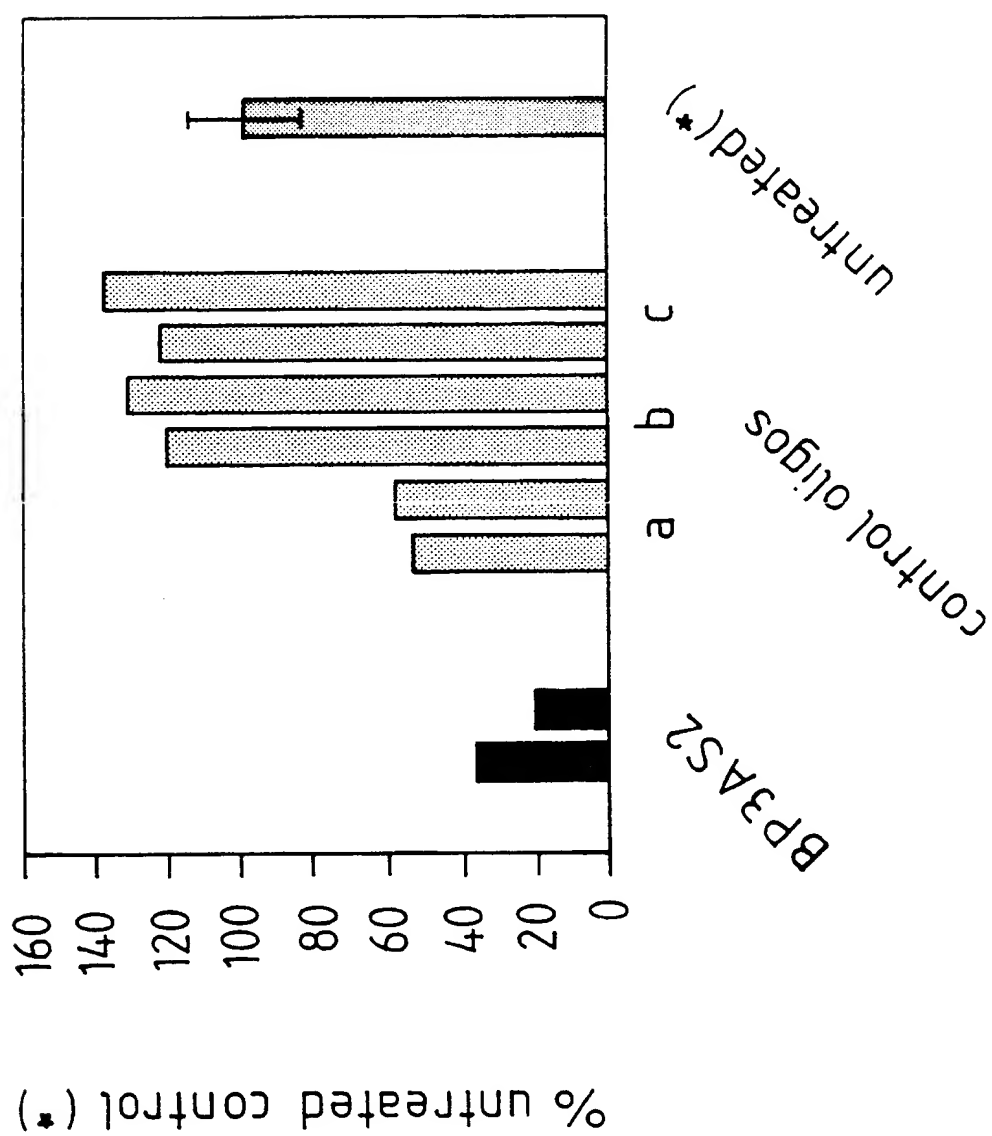


FIG. 5A

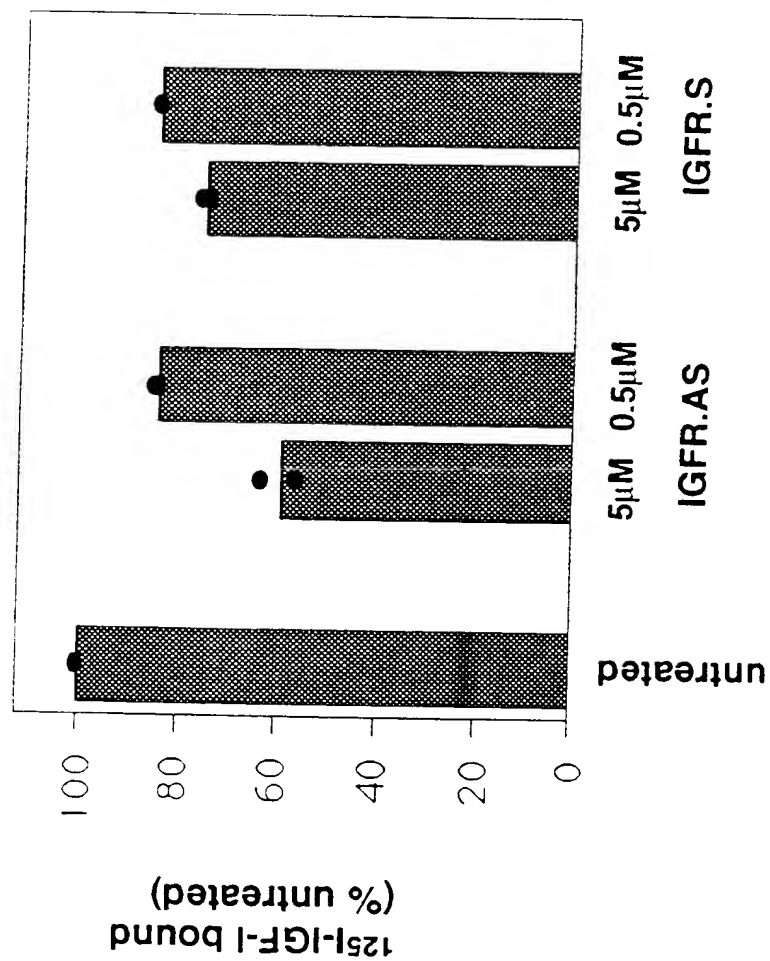
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FIG 5B



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FIGURE 6 Inhibition of IGF-I binding
by antisense oligonucleotides to IGF-I receptor



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Initial treatment with AS oligos (once daily over 2 days)

RELATIVE IGFBP-3 IN MEDIUM (scanned OD)

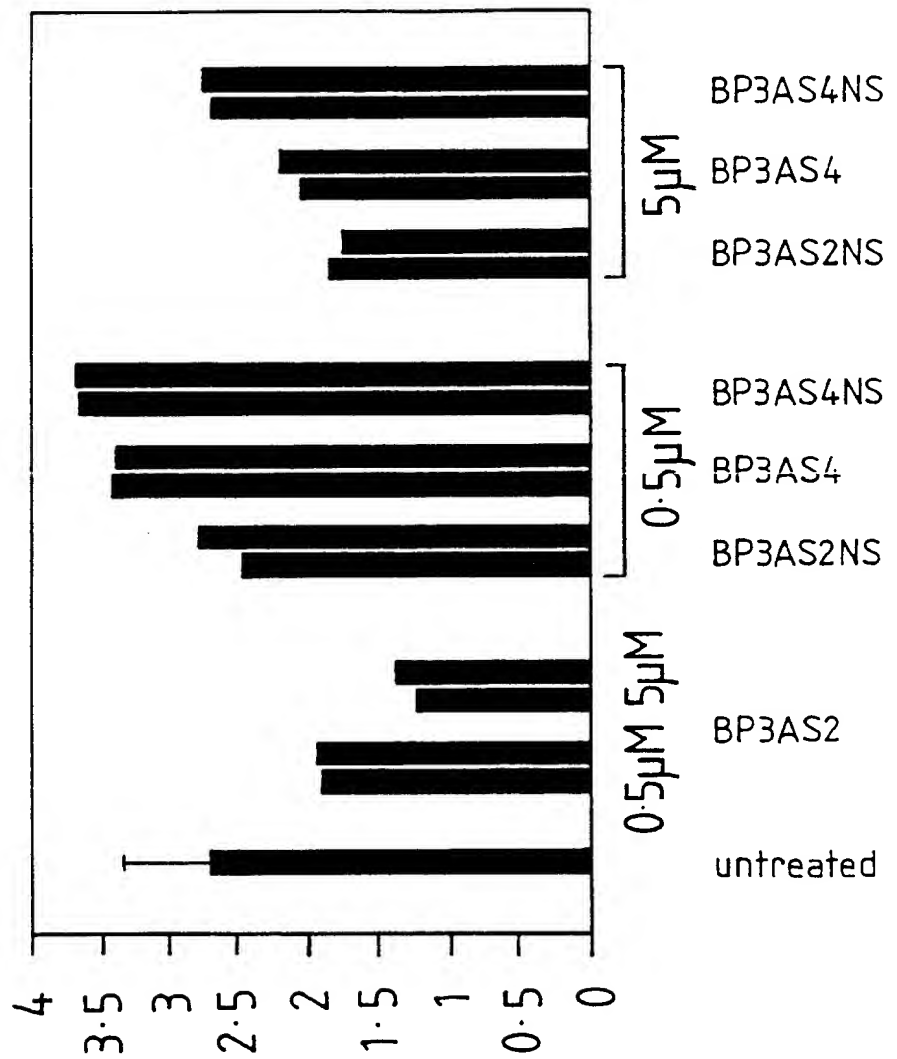


FIG 7

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Optimization of IGFBP-3 AS oligo concentration

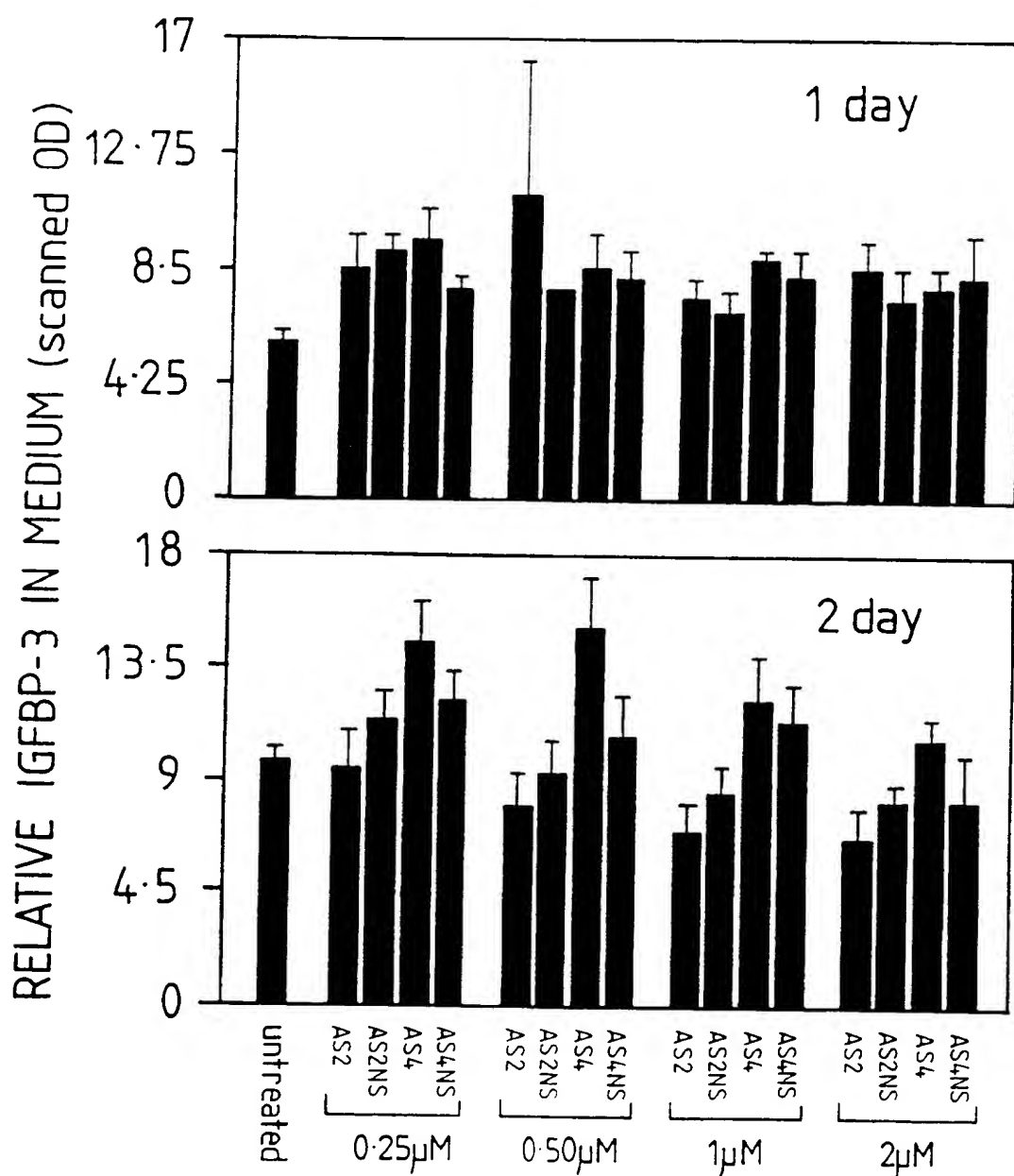


FIG 8

A. CLASSIFICATION OF SUBJECT MATTERInt Cl⁶: A61K 31/70, C07K 21/02, C07K 21/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC⁶ A61K, C07K, C12N

CHEMICAL ABSTRACTS

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See belowElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)
DERWENT WPAT; Chemical Abstracts CASM; MEDLINE; STN Genbank, Chemical Abstracts**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 94/22486 (THOMAS JEFFERSON UNIVERSITY) 13 October 1994; see whole document.	14-16, 23-24
<u>X,P</u> Y,P	Batch, J.A. et al. (1994) Localization of Messenger ribonucleic acid for insulin-like growth factor binding proteins in human skin by in situ hybridization, Journal of Clinical Endocrinology and Metabolism, vol. 79, no. 5 pages 1444-1449, November 1994	<u>23-24, 26-29</u> 1-29
Y	Cohick, W.S. and Clemmons, D.R. (1993) Regulation of IGFBP secretion and modulation of cell growth in MDBK cells, Growth Regulation, vol. 3, no. 1, pages 20-23, March 1993.	23-24, 26-29

☒ Further documents are listed in the continuation of Box C☐ See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
8 September 1995

Date of mailing of the international search report

26 SEPTEMBER 1995

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C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	Singh, P. et al. (1994) Episomal expression of sense and antisense insulin-like growth factor (IGF) - binding protein-4 complementary DNA alters the mitogenic response of a human colon cancer cell line (HT-29) by mechanisms that are independent of and dependant upon IGF-I, Cancer Research, vol. 54, pages 6563-6570, 15 December 1994.	23-24, 26-29
Y,P	Long, L. et al. (1995) Loss of metastatic phenotype in murine carcinoma cells expressing an antisense RNA to the insulin-like growth factor receptor, Cancer Research, vol. 55, pages 1006-1009, 1 March 1995.	14-16, 23-24, 26-29
X,P	Resnicoff, M. et al. (1994) Growth inhibition of human melanoma cells in nude mice by antisense strategies to the type I insulin-like growth factor receptor, Cancer research, vol. 54, pages 4848-4850, 15 September 1994.	14-16, 23-24, 26-29
Y,P	Shapiro, D.N. et al. (1994) Antisense-mediated reduction in insulin-like growth factor-I receptor expression suppresses the malignant phenotype of a human alveolar rhabdomyosarcoma, J. Clin. Invest. Volume 94, pages 1235-1242, September 1994.	14-16, 23-24, 26-29
P,Y	WO 94/23034 (Cedars-Sinai Medical Center) 13 October 1994; see "Background of the Invention" in particular.	1-29

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 12, 14-16, 21, 29
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Under rule 33.3(b) the claims relate to speculative matter and the specific search would be financially unreasonable.
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.